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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

Not a little of the work on this subject published during the past year is the outcome of researches carried out and observations made during the late war, but held back for obvious reasons until it was safe to make them public. This explains why information dated two years, and even longer, ago has only recently been given to the world.

Epidemiology.

BRUMPT (p. 4) has written an interesting article on the long-debated question of anophelism without malaria and on the spontaneous regression of malaria, showing how changes in agricultural methods may account for some instances, but by no means for all, and how, in others, the local mosquito is not attracted by man. In the same article, the author demonstrates the well-known fact that in areas long free of infection malaria may break out again if fresh gamete carriers, prisoners of war for example, are brought in.

FAUST (p. 286) published an interesting paper giving an account of the introduction of malaria into America, first by European explorers and settlers, and then by slaves imported from Africa. Later, most of the settled part became malarious, but in the south were hyperendemic centres. As agriculture developed and quinine became cheaper these areas shrank. More recently, with the economic depression of 1931, prevalence increased and this stimulated efforts at control so that, since 1933, there has been an almost uninterrupted decline. The present fear is of the possible dangers arising from the return of infected soldiers, sailors and civilians from malarious regions abroad, for *A. quadrimaculatus* and *A. freeborni* can transmit both the Pacific and Mediterranean strains of *P. vivax*.

SMITH (p. 281) attempted to appraise the value of the splenic index as a measure of malaria endemicity in southern United States, in districts with low malaria prevalence, comparing it with that of highly malarious districts. The percentages among negro children were small, 4·9 in non-malarious and 6·3 in highly malarious districts. The statement is, therefore, made that negro children should not be included in spleen surveys in southern States where the endemicity is low. Among white children, the percentages of spleens palpable

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

on deep inspiration were 12·2 in malarious areas and 10·8 in non-malarious areas but greater degrees of enlargement were found in 11·1 and 3·2 per cent. respectively. The former (spleens palpable on deep inspiration only) might be due to recent illness, chickenpox, measles, etc., and should be disregarded in places where the malarial endemicity is low. SPICER's findings (p. 282) confirm this, for the spleen rate (palpable on deep inspiration) might be as high as 15 per cent. in the absence of malaria.

A neglected aspect of malaria epidemicity—the socio-economic conditions and malaria morbidity—is dealt with in an article by BRIERLY (p. 620) as regards the State of Mississippi. The prosperity of the people depends mainly on the cultivation of cotton. In good years they can afford more and more varied food, their homes are kept in better repair, the screening is mended or renewed, and they can afford to pay for medical attention and treatment ; in bad years the reverse holds true. It is thought that these conditions suffice to explain the cyclic exacerbations of malaria every 5–6 years, characteristic of the disease in the southern United States. At the same time, it must not be forgotten that the delta region in north-west Mississippi is a flat plain with many swamps and collections of water in which *A. quadrimaculatus* breeds.

Coming nearer home, BIRRELL (p. 999) reports a case of benign tertian malaria in Londonderry, the infection having probably been contracted locally. Patients from the Services suffering from malaria were undergoing treatment and *A. maculipennis* was found breeding in the vicinity. MACNAUGHT (p. 391) records eight cases of benign tertian malaria acquired by British troops in Normandy. It is true that *A. maculipennis* occurs there, but no indigenous cases of malaria have been recorded from the locality for a long time. Infection, it is thought, may have originated in German troops stationed in Normandy subsequently to their having served in Africa, or else from others of our own troops who had previously served in malarious regions.

DOELEMAN (p. 875) has published his thesis for the degree of doctorate of medicine, Leiden University, on malaria in Middelburg between 1940 and 1945, and on parasite carriers. He covers the question of so-called " Zeeland fevers " which include typhus, enteric fevers and dysentery, as well as malaria. Other records of malaria in Europe include that of an outbreak in September 1943, which occurred in the Camargue region at the mouth of the Rhône, reported by SAUTET in *Marseille Médicale* and by SASPORTAS (p. 282). Mosquitoes, *A. maculipennis*, are abundant there and malaria is endemic, though it has not been prevalent for the past decade. Infections were by *P. vivax* and the type was clinically mild and without a tendency to relapse ; gametocyte carriers were rare, as is usual in places where malaria is disappearing. Most of those attacked were workers imported for the grape-harvest. GUHL (p. 283) records an autochthonous case in Switzerland.

DUKHANINA (p. 999) investigated the conditions under which infected persons in the Archangel Province became carriers, also the effect of treatment, the causes of repeated carrying and the density of parasites in carriers as compared with that in persons with clinical symptoms. He found that, as a rule, the carriers were those who had received insufficient drug treatment. The number of parasites in the blood of carriers is considerably lower than in acute cases ; in nine-tenths of the patients, not more than one parasite per field of the microscope could be found.

PROKOPENKO (p. 701) analyses the causes of a severe outbreak in the province of Samarkand (Middle Asia). The area involved has a high endemicity of all three types, but chiefly malignant tertian, and the vectors are *A. maculipennis sacharovi*, and, less important, *A. superpictus*, breeding in rice-fields, swamps and canals. For dealing with the situation four measures were adopted : systematic anti-relapse treatment by mepacrine, 0·3 gm. daily in a single dose ;

treatment of the entire population with 0·3 gm. mepacrine+0·04 gm. pamaquine on two successive days, repeated after an interval of five days; early detection and treatment of all acute cases of malaria and parasite carriers; and, lastly, monthly examinations of the people in order to detect carriers and to observe indices. POLUMORDVINOV (p. 283) reports endemic malaria at the limit of human settlement, more than 9,000 feet above sea-level, in southern Tadjikistan, also in Middle Asia; all three types are to be found.

MILOVZOROVA (p. 1003) shows, from an illustrative instance, that, owing to the movements of the population of the U.S.S.R. resulting from the war, there is a danger of malaria being introduced into non-endemic areas. Prompt anti-malaria measures must be taken in hand to deal with contingents brought from endemic areas.

In Las Palmas, Gran Canaria, among more than 18,000 mosquitoes captured there was no anopheline and any malaria met with there is due to infection contracted elsewhere. In other parts of the island outbreaks occur, and infection is about equal between *P. vivax* and *P. falciparum*. GARCIA SASTRE (p. 283) records an outbreak of 77 cases at the end of 1941; another of 113 in the last four months of 1942; 2,164 cases in 1943, involving eight administrative divisions; in 1944 cases were reported every month and in every week but one, with a total of 3,978 cases in 13 of the 21 *municipios*. September had most cases, 971, February and March least, 26 each. The probable vectors were *A. hispaniola* and *A. sergenti*. NÁJERA (p. 284) affirms that these are the only anophelines found in the Canary Islands.

DAS GUPTA and SIDDONS (p. 4) attribute the high incidence of malaria, 33·1 per cent., in Calcutta to the refugees flocking there at the time of the Bengal famine in 1943. In December that year the figure was 44 per cent., in November the following year 51·7 per cent., of which quartan malaria was responsible for just over 1 per cent., the rest being almost equally divided between benign and malignant tertian. The causes assigned for the prevalence are malnutrition and lack of drugs for treatment. In the North Kanara District, Bombay Presidency, malaria is, according to VISWANATHAN (p. 285) responsible for a large number of premature births, still-births and high neonatal mortality, resulting from maternal malaria; he also holds it responsible for the high infant mortality. In Haliyal this is 192 per 1,000 live-births. Deaths ascribed to "fevers" in the Punjab are largely due to malaria, especially those occurring during the last quarter of the year, after the rainy season, according to YACOB and SWAROOP (p. 285). These authors use the term "epidemic figure" to express the ratio of the average monthly number of deaths from fevers during the last quarter of the year to the monthly average for the second quarter. In years of low malaria incidence the figure approximates to unity.

Lieut.-Colonel ENGLISH and Brigadier MACCALLUM (p. 516) have given a detailed account of malaria and anti-malaria measures among the Australian Military Forces in the Borneo operations of 1945. Prior to the coming of the Japanese the incidence had been low, but with their advent mosquito control practically ceased, Japanese labour, heavily infected, was imported and malaria became rife. From different parts of the country came a similar story. For instance, in Brunei town, as the result of the efforts of an anti-malaria organization, the spleen rate in children had been reduced to 1 per cent. in the river *kampong*. When the Japanese invaded, the inhabitants fled to the hills and the rice-growing districts, and some 60 per cent. contracted malaria there. Later, they drifted back to the town, but control measures had been discontinued and malaria incidence increased. Nemesis saw to it that the Japanese themselves suffered severely and deaths from cerebral malaria—a complication practically unknown prior to this—occurred among them. Control was then again started; mepacrine for suppressive purposes was distributed and two

types of mist were used—a pyrethrum spray from aerosol dispensers, " Freon bombs," and DDT in a strength of 2·5–5 per cent. The Freon bombs were used chiefly indoors, 4–12 seconds' spraying per 1,000 cubic feet, and they were particularly effective against *Aëdes*. Out of doors, the following methods were adopted : a man walked along bush tracks at the rate of a yard a second with a discharging dispenser in each hand, or the apparatus was placed on the ground at 15-yard intervals and allowed to discharge for 60 seconds. The DDT mist was used out of doors only, by means of an American 3-gallon decontaminator pressure sprayer with a nozzle of 0·08 inch aperture.

HUNTER (p. 293) analysed nearly 3,000 cases of fever in a hyperendemic malarial area on the Assam-Burma border. Malaria proved to be the cause in 76 per cent. ; another 3 per cent. were diagnosed on clinical grounds only. As regards types of infection the percentages were : among British troops *P. vivax* 64, *P. falciparum* 30, mixed 6 ; among Indian troops, 47, 43 and 9 per cent. respectively. One per cent. of quartan is given for each [which would bring the British total to 101 per cent.]. The lower prevalence of *falciparum* infections among the British troops may have been due to their having taken suppressive mepacrine. If blood smears gave persistent negative findings (*i.e.* three successive negative smears) adrenaline was found useful. Sternal puncture, though performed 20 times, was said to be of no use as a diagnostic aid [but see SCHULTES (p. 199)].

The Union of South Africa issued in 1941 a map showing its malarious areas (p. 999). By means of different colours four areas are depicted : (1) In which the risk is continuous—the East Coast near the border of Mozambique. (2) In which the disease is serious and in which epidemics occur during the summer—the north and east parts of the Union. (3) In which successive outbreaks occur each year, but mild in character—to the south and west of the second area. (4) In which occasional epidemics occur—to the south and west of the third, but reaching Pretoria, Witbank, Newcastle and Durban.

According to LE GALL (p. 284), in 1941 malaria was very severe in Madagascar, owing to exceptional rainfall ; one-third of all patients treated were suffering from this infection. The disease was found to be endemic in all the islands of the Comores Archipelago, to the west of the northern tip of Madagascar, but varying in degree. In Mayotte, spleen rates varied between 40 and 90 and parasite rates from 10 to 18 ; in Moheli the former was 50 to 80 and the latter 20 to 35. Anjouan is least affected, with spleen rates from 20 to 55. The vectors are *A. gambiae* and *A. funestus* ; *A. mauritianus* is also found, but is not a vector. In Grande Comore the chief breeding-places are the tanks supplying the villages with water.

Turning next to West Africa, American troops, most of them coloured (five coloured to one white) were, in 1942, stationed in a malarious region of Liberia. The parasitic index of the indigenous infants was 80 to 90 per cent., all *P. falciparum*, and *A. gambiae* abounded. Suppressive quinine, 40 grains a week, was given and half to three-fourths of the troops took it regularly for the first five months. Nevertheless there were 54·8 per cent. attacked during eight months, 38·8 per cent. initial attacks and 16 per cent. subsequently. A second batch of troops (three coloured to one white) arrived later and lived in better conditions, but for four months were given no suppressive treatment. The malaria rate among them was higher, initial attacks 86·3 per cent., subsequent attacks 58·1 per cent., or a total of 144·4 per cent. as recorded by MOORE (p. 4).

A malaria survey in Wagadugu, the capital of Mossi in French West Africa, by LE GAC and his colleagues (p. 621) in 1942, after a severe outbreak there, showed that among nearly 3,000 children under 12 years of age there was a spleen rate of 37·15 per cent. and a parasite rate of 53·67 per cent. *A. gambiae*

was the chief vector, but *A. funestus* and *A. nili* were also present and the main breeding-places were the *marigots*—rivers that lose themselves in the ground—which became dried up at some seasons, but flooded in the rains. Some of these are brought into service, by damming, to provide water at all seasons.

RIBBANDS (p. 621) has made an interesting observation on the association of moonlight with the house-haunting habits of the female anopheline *A. funestus*, in Sierra Leone and near Sekondi in the Gold Coast. He found that during moonless periods the flighting of *A. funestus* was partially inhibited and when the moon came out they entered in numbers four or five times as many as on a moonless night. Also, they were observed to rest on the wall of the hut before beginning their meal and this may explain how residual DDT on walls is able to protect the occupants of a room against being bitten, the insects being incapacitated during the preliminary short resting period. It is probable that *A. gambiae* acts and suffers in the same way, but enough information on this has not been obtained for arriving at a decision.

The same author (p. 904) has carried out some experiments in the West African bush from which he concludes that bush-clearing around dwelling-places is not a justifiable measure for reducing anopheline infestation, at least in so far as *A. funestus* and *A. gambiae* in West Africa are concerned.

MELVILLE and his colleagues (p. 92) have recorded the results of surveys in several localities in Abyssinia, mainly in the Rift Valley region. North-west of the valley they found practically free from malaria, because the temperature is too low. There are highly endemic areas near Lake Chercher and also in the Dawa Parma and Ganale Doria river valleys, but the area which includes Mega, Moyale, Adola and Ghimir has generally a low endemicity. More than a dozen species of Anopheles are present, but the chief vector is *A. gambiae*. *A. pharoensis* and *A. d'thali* are possible vectors.

HENDERSON (p. 287) has written an article containing a general survey of malaria conditions prevailing in the Guianas and the Antilles and points out that there is a good opportunity and field there for research into several unsolved problems. KENNY, in an appendix to a report on British Guiana by GIGLIOLI (p. 286) shows forcibly how houses badly screened become mosquito-traps. At a mining centre on the Berbice River many people lived in screened wooden houses with cracks in floors, walls and roofs, and where the doors were carelessly left open. Mosquitoes could be captured by the hundred in these houses and 83 per cent. were anophelines and nearly all of these *A. darlingi*. The occupants had a blood parasite rate of 36 per cent. and many were carriers of gametocytes. Among the *A. darlingi* dissected 88·8 per cent. contained oöcysts. Institution of daily mosquito-catching and treatment of human carriers reduced the percentage of infected mosquitoes to less than one per cent.

FLOCH and DE LAJUDIE (p. 704) estimated the endemic indices of malaria in the interior of French Guiana and in Cayenne to be: spleen rates 44 and 12 respectively, parasite rates 24 and 6, and gametocyte carrier rates 7 and 0·3.

Little seems to be known about malaria in the Amazon Valley of Brazil; hence the value of a report by CAUSEY and MELLO (p. 287) of two surveys carried out, one in December 1942, when infection rates are expected to be low, the other in June 1943, at the end of the wet season. The parasite rate, strange to say, was lower in the second, 3·3 per cent. among 27,103 examined, than in the first, 5 per cent. among 19,629. The explanation probably is that after the first survey atebrin had been widely distributed and anti-mosquito work undertaken. The chief vector is *A. darlingi*.

SOTO (p. 815) records a survey he made in the Medellin Valley and Itagüi, Colombia, 1,500–1,950 metres above sea-level. The spleen rate among 3,700 individuals between 5 and 19 years of age was 22·1 per cent. Infection is mainly by *P. vivax*, being eight times as frequent as that by *P. falciparum*.

A. pseudopunctipennis and *A. argyritarsis* breed abundantly, the latter contributing more than half the total anopheline larvae identified. Nevertheless, the chief vector is neither of these, but *A. punctimacula*, which predominated in captures in human dwellings.

CALDWELL (p. 1104) remarks on the varying intensity of malaria in different districts of the Santo Domingo part of Haiti; spleen rates in different communities ranged from 0 to 42·8 per cent. *P. falciparum* infection was found to be the most common, 72·8 per cent., *P. vivax* accounting for 17·1, *P. malariae* for 4·7 per cent., and the remainder were mixed strains, among nearly 1,400 positive blood smears examined. *A. albimanus* is the principal vector.

Aetiology.

BLACK (p. 816) publishes a preliminary note on the cultivation *in vitro* of New Guinea strains of human malaria parasites. He places 20–30 cc. of blood in a large test-tube containing 0·1 cc. of 50 per cent. glucose and stirs it until defibrination is complete. The serum is separated by centrifuging and is placed in a flat-bottomed tube, ½ inch in diameter, to give a column 1½–2 inches in height. Red corpuscles with *P. falciparum* are obtained from beneath the leucocyte layer after centrifugation and introduced into the bottom of the serum tube and incubated at 37°C. Within 28 hours schizogony was observed, together with the invasion of new cells and in 78 hours gametocyte-like forms appeared.

RAFFAELE (p. 1016), in an article on the biology of the malaria parasites, claims to have demonstrated exo-erythrocytic stages of development in all three human parasites, chiefly in sternal marrow taken from patients a few days after they had been infected by sporozoites. In the case of *P. malariae* he has demonstrated such forms a year after infection. Incidentally, this fact may account for the failure of certain drugs to prevent infection by sporozoites, though active in the erythrocytic stages of development.

BRUG (p. 288) describes certain intracellular bodies seen in smears of the lung from a case of general paralysis ending fatally ten days after intravenous injection of *P. vivax*. WENYON agrees with the author that they *may be* exo-erythrocytic forms analogous to those seen in avian malaria.

Transmission.

Descriptions of the species of anophelines to be found in certain countries or districts with keys for their identification have been published: for Malaya by the Federated Malay States Institute for Medical Research (p. 1106); for Syria and Lebanon by BERBERIAN (p. 1105); for Grand Canary, particularly the two chief species *A. hispaniola* and *A. sergenti*, by NÁJERA (p. 284); for Ecuador by CASTELLO (p. 262); and YAO (p. 391) has published a synopsis of the epidemiology of malaria in China and has given a list of 37 species of *Anopheles* found in that country and the geographical distribution of each of them. Seven are recognized vectors of malarial infection, namely: *A. minimus*, *A. jeyporiensis* var. *candidiensis*, *A. maculatus*, *A. hyrcanus* var. *sinensis*, *A. pattoni*, *A. maculipennis* var. *atroparvus* and *A. sacharovi*. BELKIN and his colleagues (p. 6) have drawn up a key for identification of Solomon Islands mosquitoes and discuss the taxonomy, distribution and biology of each species.

ROZEBOOM and KNIGHT (p. 817) have taken in hand an investigation to elucidate the relationships of closely allied but distinguishable groups of mosquitoes, designated hitherto as " varieties " of species, basing their conclusions on biometric data derived from examination of series of specimens.

KEENER (p. 197) has written a detailed account of the life-history of *Anopheles quadrimaculatus*, kept under nearly constant conditions as to air temperature, 76°–80°F., and high humidity. He observed that though the sexes emerged in

almost equal numbers the males emerged before the females. The average time taken from oviposition to emergence of the adult was 21 days and females survived up to 62 days. The hour for pairing was usually about 8 p.m. The female takes up 3 mm. or so of blood at a feed and may do this more than once in the 24 hours. She may lay 9–12 batches of eggs and 200 or more per batch. Professor BUXTON adds a note that this is not consistent with the statement that the insect may produce 3,000–4,000 eggs and also that those who maintain colonies of *Anopheles* know that differences between successive experiments are often great. BRADLEY and FRITZ (p. 198) have noted the seasonal occurrence and abundance of this mosquito. In the warmest zones (70°–75°F., in Florida, Southern Texas and Louisiana) they may be met with all through the year; the same holds good fairly generally at 65°–70°F., but below this, at 60°–65°F. they are not found in the houses during the winter months. Their range of flight has been investigated by EYLES and his colleagues in South Carolina (p. 199); it was often two miles and might extend to 3·6 miles as measured in a straight line. HUFFAKER and BACK [this *Bulletin*, 1945, v. 42, 687] found that in Delaware it rarely moved more than a mile from its breeding-place, but that a few might travel as far as three miles.

METCALF (p. 198) found that the salivary glands of the female of this species contain agglutinins for the corpuscles of man and other mammals, but not for chicken or turtle blood, acting at 1 : 1,000,000; and an anticoagulin active at 1 : 10,000; both are thermolabile. The glands contain no digestive enzymes.

PAL (p. 518) contributes a valuable paper on the bionomics of *A. culicifacies*. It appears that the female will oviposit in tap water, ponds, muddy waters, tanks, irrigation channels and in polluted, stagnant, or pure water; in short, in all except soapy water. For other details of its ecology, of interest to entomologists and malariologists, the original should be consulted. Analogous information regarding *A. fluviatilis* is furnished by RAO (p. 519) and on *A. maculipennis* in Northern Iran by ZOLOTAREV (*ibid.*) MOHAN (p. 197) gives an account of his method of maintaining a laboratory colony of *A. fluviatilis*. Eggs obtained from wild-caught females were floated in waxed cork-rings in mud-lined enamel bowls. Hay infusion or brewers' yeast, or a mixture of litmus milk, 2 parts, and dehydrated serum, 1 part, was added to the water as food for the larvae. Pupae were removed to bowls of clean water in a cage. For adults, glucose water on cotton wool was available and a rabbit with its back shaved was placed in the cage each night.

CAMBOURNAC and SIMÕES (p. 95) have investigated the propagation of Anopheles in the rice-fields of Aguas de Moura district, a hyperendemic area where *A. maculipennis atroparvus* is the vector of malaria. *A. claviger* is present but it does not associate with man or his domestic animals. The length of life of the former, *A. m. atroparvus*, under natural conditions seems to be 1½–2 months, and at the height of the breeding season each hectare of rice-fields can produce up to 35,000 anophelines a day.

Egg-structure is not a satisfactory criterion for distinguishing the type forms of *A. gambiae* from the variety *melas*. CHWATT (p. 5) has tried to differentiate them by their respective bucco-pharyngeal armatures, but differences observed between individual specimens were not consistent.

FLOCH and ABONNENC (p. 702) found that *A. darlingi* is the chief vector of malaria in French Guiana and 91 per cent. of the Anopheles taken in houses throughout the year—the observations were made in 1943—were of that species. It is not, however, found in Cayenne where *A. aquasalis* is the chief house-frequenter.

Anopheles lungae, *A. tessellatus* and *A. longirostris* are closely related, but the larvae of the two first are distinct and STONE (p. 6) has described characters which distinguish the females; their distributions also differ. *A. lungae* occurs

only in the Solomons, *A. longirostris* in New Guinea and New Ireland, *A. tessellatus* from India to Hong Kong, in the Netherlands Indies, the Philippines and the Moluccas.

OWEN (p. 6) has described the larva and adults of a new species of mosquito in the Solomon Islands, Guadalcanal, *A. koliensis*. It frequents human habitations and consequently is an important transmitter. Morphologically, it occupies a place intermediate between *A. punctulatus* and *A. farauti*, but the taxonomic relationships of the *punctulatus* group are obscure. DAGGY (p. 1107) has detailed the biology and ecology of *A. farauti* (formerly known as *A. punctulatus moluccensis*), the chief vector of malaria in Australasia. It is also a vector of *Wuchereria bancrofti*, complete development having been followed in it.

ZUKEL (p. 7) recommends anthracene (blue), rhodamine (red) and fluorescein (green fluorescence) for marking mosquitoes for rapid identification under ultraviolet light. The first is used as an aerosol and 10 mgm. per litre of air is harmless ; as a dust it is mixed with twice its quantity of gum arabic, water is added and the mixture is evaporated to dryness and ground up. The mosquitoes, after being dusted, are placed for 15 minutes in a saturated humid atmosphere. The other two preparations are used as dusts in a similar way, but with these the formula is 10 mgm. of the dye to 3 gm. of the gum.

BISHOP and GILCHRIST (p. 710) describe a method which they have devised for obtaining sporozoites free from glandular tissue by inducing mosquitoes to eject them through membranes of chicken skin.

YOUNG *et al.* (p. 5) have shown by experimental means that *P. vivax* imported from the Pacific, the Mediterranean and South America is readily transmitted by local American mosquitoes in Colombia, San Francisco and Texas. MOORE and his colleagues (p. 1002) have also tested four species of Californian Anopheles, *viz. A. maculipennis freeborni, A. m. occidentalis, A. pseudopunctipennis franciscanus* and *A. punctipennis* to find out whether they would transmit malaria, mostly *P. vivax*, acquired in the Pacific by soldiers who had returned to California. He found, as had others, that they were ready vectors.

Malaria in Borneo was for years believed to be carried mainly by *A. maculatus*, but in a survey made in 1939 a village was found relatively free from malaria, although this mosquito abounded there. Further study by MCARTHUR (p. 1000) showed that this species is to a great extent zoophilic, whereas *A. leucosphyrus*, which was also present, was strongly anthropophilic and those dissected were found to be infected. More investigation was then undertaken and *A. leucosphyrus* proved to be the most widely distributed mosquito in Borneo. It has escaped incrimination so long because of its elusiveness. It enters houses after midnight, feeds on the sleeping occupants and leaves again before dawn and consequently is rare in daytime catches. It breeds entirely in the jungle and is easily controlled by clearing round its breeding-places. The assumption had been made that the epidemiology of malaria in Borneo was the same as in Malaya, whereas the reverse was the fact ; in Malaya, clearing of the jungle leads to the introduction of *A. maculatus* and the cleared area becomes malarious.

A. punctimacula D. and K., formerly regarded as incapable of, at least as not engaged in, transmitting malaria, because the parasite could not be demonstrated after the insects had fed on infected persons, has been shown by HUFFAKER, SOTO and REY (p. 392) to be a capable vector. Another unexpected finding, and this time a negative one, is that recorded by GARNHAM (p. 291) concerning *A. pharoensis* in Kenya ; though it is present in the Colony, though it enters huts during the night and though it feeds on man and its length of life is sufficient to allow of development of infection, nevertheless it is not a vector of malaria, at all events not an important one in Kenya.

Wilson, M. E. and Wilson, D. B. (p. 97) made examinations fortnightly of the blood from 137 African soldiers stationed in a hyperendemic area of East Africa. Here the soldiers were exposed to frequent reinfection by alien, if not new, strains of malaria parasites. Only three of them showed more than 10 crescents per 500 leucocytes; eight had from one to four per 500 and twenty-eight had less than one. Assuming, say the authors, that at least one crescent per 500 leucocytes is necessary for successful infection of a mosquito, the conclusion is reached that not more than one per cent. of the soldiers became at any one time a probable infector.

In contradistinction to *A. funestus*, which bites almost entirely at night, *A. dureni* is a common day-biting mosquito near Elizabethville, in the Belgian Congo, and may be found in human dwellings, but is more abundant in trees near water and its favourite breeding-places are shaded sections of rapid streams. It seems never to bite at night, but it is a capable malaria vector, according to Vincke and his colleagues (p. 291).

In Trinidad, Downs and Pittendrigh (p. 1001) record that plantations of cocoa have replaced forest and the cocoa trees are protected by shade trees, immortelles, *Erythina glauca* and *E. micropteryx*, and these immortelle trees are heavily parasitized by bromeliads, more than 60 per tree on an average; *Anopheles bellator* selects the bromeliad as its host-plant. This mosquito attacks the plantation workers, especially on damp days, or on the verandahs in the evening. Occasionally, it enters the building to feed but leaves for forest cover directly afterwards. Manual removal of bromeliads is costly and, indeed, not very practicable; they can be got rid of by spraying with copper sulphate solution. If the proposal of the Trinidad Government to abandon shade trees and protect the cocoa by rows of trees planted perpendicular to the prevailing wind should succeed, endemic bromeliad malaria should disappear from the centre of Trinidad.

Transfusion Malaria.

Sharnoff, Geiger and Selzer (p. 1002) record two cases of accidental transmission of malaria by blood transfusion. In one, the blood used had been stored for eight days and all attempts to detect the parasite, *P. malariae*, in the donor's blood failed. In the other, the donor had had fever in Porto Rico two years before. Clearly, storage of blood for eight days is no safeguard against infection, and it would be wiser not to use for transfusion blood from any person who had come from areas known to be malarious. Rubenstein *et al.* (p. 292) have related cases arising after much longer periods than the last. In a paper stressing the hazards of transfusion malaria, they record five cases in which the time which had elapsed since the donor was last in an endemic malaria region was determined and it was found to range between 12 and 27 years. The interval between the transfusion and the onset of symptoms varied from 10 days in the case of *P. vivax* to 111 days with *P. malariae* infections. They point out that the dangers are all the greater now that many potential donors have served in malarious regions abroad. The same risk is indicated by Talice and Mackinnon (p. 292) who report two cases, both *P. malariae* infections. One of the donors had acquired his infection in Africa nine years before, the other in Italy seven years before. Incidentally, Nagley (p. 296) reports what seems to be a relapse of *P. falciparum* infection after 17 years.

Pathology and Immunity.

Thonnard-Neumann (p. 520) has studied the blood and the bone-marrow in all three forms of human malaria infection and the pathogenesis of malarial anaemia, as it affects the red corpuscles, the reticulocytes and the haemoglobin. He did not find any increase in reticulocytes in the peripheral blood during the acute attacks, although they did increase in the bone-marrow; in other words,

the plasmodia interfere with discharge of reticulocytes from the marrow into the circulation. This inhibition ceases when the plasmodia disappear from the blood stream. In short, the anaemia in benign tertian and in quartan infections (there was only one *falciparum* infection among his cases) developed mainly from destruction of red corpuscles by the plasmodia and was associated with an inhibition of the discharge of young cells from the marrow.

Diagnosis and Tests.

PERRET-GENTIL (p. 96) examining the blood of Italian and Yugoslav refugees in Switzerland found that four or five thin smears superimposed—each being dried by waving the slide in the air before the next smear is spread—were better than the ordinary thick-drop method for diagnosis. Such examination proved, in their experience, quite as serviceable as sternal puncture, if not more so.

PACKER (p. 1108) finds that dark-ground illumination is a useful and rapid method for diagnosis of *P. vivax* infection, owing to the brilliant refractiveness of the pigment which is in active Brownian movement. It is less satisfactory for *P. falciparum* because of the paucity of pigment in the young ring forms. SCHULTES (p. 199) demonstrated the value of sternal marrow smears in the diagnosis of malaria after repeated failure to find the parasites in blood smears. HUNTER (p. 293), as stated already, is of a different opinion. Schultes maintains that the procedure is useful also for prognosis as regards the likelihood of relapse occurring and for judging the fitness of soldiers for service after recovering from an attack of malaria.

ROGERS (p. 392) has evolved a technique for concentrating malaria parasites in a sample of blood and so facilitating diagnosis. The procedure is too complicated for description here; briefly the blood is centrifuged in a small tube and the packed red corpuscles with some serum are withdrawn with a capillary tube and blown on to a slide and a film is made. Those interested should consult the original paper for details.

Identification of malaria parasites by means of the fluorescence microscope is described by METCALF (p. 392). Thin blood films, after fixing, are stained with berberine sulphate or rivanol. The fluorescence microscope shows them up luminous and thus renders their detection easy. The simplicity of the method favours its use in routine malaria surveys.

DULANEY and WATSON (p. 818), using an antigen from pooled *P. knowlesi* parasites from monkeys, found the complement fixation test more sensitive than blood examination in detecting persistent subclinical infections; the patients had all received suppressive treatment with atebrin. In over 6,000 coincident examinations 62 per cent. were positive by complement fixation, only 13 per cent. by film, and in cases of relapse the complement fixation : blood film ratio was, on the day of attack, 0·7 : 1; after three days 16 : 1 and after six days 80 : 1.

Mention may be made here of the Weltman Coagulation Reaction which, though not specific, is considered of value in the diagnosis of tropical fevers. It is a protein-globulin reaction. To each of a series of ten small test-tubes containing graduated ascending dilutions of calcium chloride solution is added 0·1 cc. of haemoglobin-free serum. The tubes are then shaken and placed for 15 minutes in a boiling water-bath and the reading taken and noted as clear, faintly opalescent, turbid or flocculating. Normally, the first six tubes show flocculation, and coagulation in No. 6 or 7 is regarded still as normal, but coagulation beyond this, in 8, 9 or 10—a shift to the right—is held to indicate an acute inflammatory exudative process. Haemolysis may account for such a shift in malaria; the test is, therefore, helpful in blackwater fever and, if repeated during the course of disease, may assist in forming a prognosis (KLEEBERG, p. 393). Another blood protein test, the protein tyrosine reaction

(euglobulin), is said by WARTMAN and SHLIMOVITZ (p. 1003) to be of limited, if of any, value in diagnosis. They found that two-fifths of those with positive blood films have a normal euglobulin value. They affirm that it is valueless also in predicting relapse. The reading may be high in patients with acute epidemic hepatitis and the high readings seen in malaria patients return to normal in a few months.

FENTON and INNES (p. 298) describe a modification of the Field method of staining malaria parasites in thick blood-films, the films being dehaemoglobinized during the staining which is completed by immersion for 10–15 minutes in a corrective Leishman solution. Three staining solutions are used; the details of the technique cannot be given here.

That false complement fixation reactions for syphilis may be given by malaria patients has been recorded again and again, but BABIN and DULANEY (p. 297) have shown that syphilitic sera may be a cause of false complement fixation reactions for malaria when a phosphate buffer extract of *P. knowlesi* is used as antigen. High-titred syphilitic sera give these reactions more often than do low-titred sera. In syphilitic patients treated with malaria, the malaria complement fixation became positive about the time that the first positive blood film was seen. A noteworthy feature was the relation between the fluctuations in the malaria and the syphilis complement fixation titres.

ROBINSON and MCKINNEY (p. 298) carried out the complement fixation test for syphilis with the sera and cerebrospinal fluids of 100 non-syphilitic soldiers suffering from *P. vivax* malaria. The serum was positive in 33, doubtful in 11; all became negative after ten weeks. They had been given mepacrine as soon as the malaria was diagnosed. The spinal fluid was negative to the Kahn test in all.

The Cephalin Flocculation Test was tried by MAKARI (p. 623) in 105 cases of malaria infection, both *vivax* and *falciparum*, and he found it positive in 96 (91·4 per cent.). When antimalaria treatment was given the test tended to become negative. The suggestion is made for this test to be used on cerebrospinal fluid in cerebral malaria and as a routine in prospective blood donors.

LIPPINCOTT *et al.* (p. 523) carried out some liver function tests in a number of patients suffering from *P. vivax* malaria, namely bromosulphthalein retention, cephalin flocculation, galactose tolerance among others, and concluded that there was transient disturbance of liver function during the attacks, but there was little, if any, indication of permanent damage.

DOLE and EMERSON (p. 624) have shown that the changes in plasma protein are not specific in malaria, as PROSKE and WATSON had thought [see this *Bulletin*, 1939, v. 36, 813] and, therefore, diagnosis cannot be based upon it. The total protein, they found, remained within normal limits during the malarial attack, but the albumin globulin ratio was lowered and the increase in globulin occurred mainly in the fibrinogen and γ globulin fractions.

The measurement of blood oxygen in malaria has been determined by YAN TIM WONG (p. 9), with the use of Millikan's oximeter. During the cold stage, owing to the hyperpnoea, the oxygen-saturation increased slightly; as the temperature rose the percentage saturation fell and, if the paroxysm was a severe one, a 70 per cent. saturation only might be reached. Inhalation of pure oxygen and intravenous injection of 300–600 cc. of red corpuscles did not compensate for the reduction.

JARCHO (p. 3) in a paper on the history of malariology points out that, in spite of increase in our knowledge of malaria, eradication of the disease progresses very slowly; he thinks that immunological methods are more likely to achieve this end. In this connexion it is to be noted that TALIAFERRO (p. 414) has studied the question of immunity in malaria. He shows that attempts at producing artificial immunization, passive or active, succeed in some degree in

monkeys and birds, but that in man the results are meagre, though the procedure may be an adjuvant to treatment by drugs. Relapse, it is thought, may be due to the persistence of exo-erythrocytic stages during latency. It is noted that other serological changes occur in the course of malarial infection—production of precipitins, agglutinins, and complement-fixing substances. As regards the last, the reaction depends on a genus antigen, thus differing from strain-specific immunity, and antigens for this reaction in man may be prepared from *P. knowlesi* and *P. gallinaceum*.

Shannon *et al.* (p. 11) showed chemically that mepacrine is localized chiefly in the liver and less in the spleen, kidneys and leucocytes. Jailer (p. 11) determined by means of the fluorescent microscope that most was stored in the liver parenchyma cells and little in the Kupffer cells, none in the sinusoids; in the spleen in the Malpighian corpuscles and in the kidney in the convoluted tubules. Oldham and Kelsey (p. 11) in a pathological study of mepacrine in fowls and rabbits showed that the former excreted the drug more quickly than did the latter. In both animals most of it was stored in the liver, having regard to the relative sizes of the organs. The toxicity of mepacrine is three times as great for rabbits as for fowls. In pregnant rabbits the drug could traverse the placenta and be stored in the foetus.

Clinical.

Shute (p. 8) has written a paper on the clinical features of malaria which is of particular value in view of malaria infection in returned soldiers; and Coggeshall (p. 295) showed, from observation of more than 3,000 returned service men, how prone the Pacific strains of *P. vivax* are to cause relapse; 57 per cent. had had more than 14 acute attacks and some had had as many as forty. Splenomegaly was not marked and anaemia and cachexia were absent. Further, in regard to Pacific strains of this plasmodium Noe *et al.* (p. 521) demonstrated that, by leaving a certain number of patients infected with *P. vivax* to remain untreated, the cyclic recurrence at regular intervals, observed in chronic *vivax* infections treated with mepacrine in the south-western Pacific, occur but rarely, if at all.

Heilig (p. 520) contributed an interesting article indicating the many conditions which malaria may simulate or perhaps it would be more correct to say, many conditions which are basically malarial, such as pneumonia, pleurisy with effusion, coronary thrombosis, hepatitis, biliary colic, dysentery and nephritis. Most and Hayman (p. 1004) mention some unusual clinical manifestations of *P. vivax* infections; for example, signs indicative of abdominal disease, meningitis (stiff neck and fever), convulsions, urticaria, angioneurotic oedema, symptoms of pneumonia; also, trauma and surgical operations may reactivate malaria. Some of these unusual forms of malaria may lead to unnecessary surgical operations being undertaken, but it must not be forgotten—and this adds to the difficulty—that the presence of malaria does not exclude the possibility of other conditions coexisting. Kaplan (p. 296) records the case of a man intermittently, in fact almost continuously, incapacitated by severe headaches. He had suffered much of many physicians, had had Kahn tests carried out repeatedly, had undergone psychiatric and physical examinations, had had teeth extracted, but for two years and even longer had not had his blood examined. Finally, this was done; *P. vivax* was seen, quinine and atebrin given and cure followed.

Laha (p. 9) reports two cases of malaria [type not mentioned] associated with signs of nephritis. One cleared up rapidly on small doses of quinine; the other patient improved temporarily, but died of uraemia a month later. [The association of nephritis and quartan malaria was noted years ago by

Giglioli in British Guiana. See this *Bulletin*, 1930, v. 27, 508, for a review of Giglioli's book *Malarial Nephritis*.]

Tumulty *et al.* (p. 819) investigated the organic and psychological effects of recurrent malaria in a number of soldiers, but found no evidence that attacks of recurrent *P. vivax* malaria, even when numerous, caused damage or dysfunction of the organ systems, apart from the general debility, but soldiers developing early in the disease symptoms more characteristic of chronic infection—anorexia, indigestion, insomnia—should be removed from units where marked physical exertion is called for, because of the effect on morale. Hospitalization tended to foster the development of neurotic patterns.

Andrew (p. 522) observed a number of cases of *P. vivax* infection in which the patients complained of sudden acute pain in the left upper quadrant of the abdomen, or in the epigastrium and, at times, at the tip of the acromion process of the left shoulder. The pain was accentuated by deep breathing and there was tenderness in the left hypochondrium. The most likely explanation is a sudden stretching of the capsule of the spleen due to localized haemorrhage, the shoulder pain being caused by diaphragmatic irritation.

Bystrov (p. 294) records more cases of a fulminating and fatal type of "benign" tertian malaria to which he first called attention nearly 20 years ago. Most of the cases occur in patients between 4 and 16 years of age. The attack is accompanied by repeated vomiting, followed by loss of consciousness, convulsions and death. The spleen is enlarged and there is cerebral oedema; the fatal termination is attributed to the latter and the increased intracranial pressure resulting therefrom. *P. vivax* is seen in smears of the blood and of the organs, most in the schizont stage.

Jennings (p. 623) puts on record yet another case of serious malaria (cerebral with coma) in a man who, having for months while in a malarious district taken his prophylactic dose daily, leaves it off when departing from his station for England. He had a heavy malignant tertian infection.

Osgood (p. 92) relates cases of malaria, *P. vivax* infections, in women living in Oregon State, where malaria till then had not been known. A soldier, a relative of one of the patients, had returned from the Pacific where he had contracted malaria and was living in a tent 50 feet away. *A. maculipennis* was common in the neighbourhood.

Raper *et al.* (p. 8) describes cases in African natives in which, in spite of dividing forms and mature schizonts being seen in the peripheral blood, the infection was running a mild course. The patients were immune, or partially immune, coming from districts where malaria transmission occurs for a short period annually. In one case, for example, no treatment was given, yet the temperature became normal on the fifth day and no parasites were seen in the blood after the seventh day.

Psychotic conditions including depression, anxiety, mania, hallucinations, delusions and even suicidal tendencies occur in infections by *P. vivax* or *P. falciparum*, as recorded by Büssow (p. 297); the duration of attack is variable, but even when they are prolonged the outlook is favourable.

Prokopenko (p. 8) carried out observations on three estates of Uzbekistan (Middle Asia) where outbreaks occurred affecting practically all the people. Most suffered from subtertian infection, but many had benign tertian parasites as well; quartan was rare. All were treated with acriquine (mepacrine) and plasmocide (pamaquine) and mosquito breeding-sites were attended to. The main source of infection appeared to be symptomless carriers.

Bookless and Naftalin (p. 199) record once again the unusual, or at least the unexpected, mildness of typhoid fever when concomitant with malaria. In the early stages all indications of so serious a disease as typhoid fever may be absent and early diagnosis is postponed by the finding of malaria parasites.

But, though the parasites disappear with antimalaria treatment, symptoms continue—rose spots, pea-soup stools, etc. It is to be noted that antimalaria drugs are no obstacle to the success of haemoculture for *Bact. typhosum*. SCOTT (p. 200) remarks in comment that the peculiarities, in particular the mildness of the attack, of this association of malaria and typhoid fever had been noted more than a quarter of a century ago by MANSON and Almroth WRIGHT, and he refers to a paper relating in detail several cases under his own observation [see this *Bulletin*, 1920, v. 15, 252]. *H. Harold Scott.*

[*To be continued.*]

MALARIA.

SAPERO, J. J. **The Malaria Problem Today : Influence of Wartime Experience and Research.** *J. Amer. Med. Ass.* 1946, Nov. 16, v. 132, No. 11, 623–7.

FALCON TREJO, A. Paludismo en el ambiente rural. [**Malaria in a Rural Environment.**] *Med. Colonial.* Madrid. 1946, Apr. 1, v. 7, No. 4, 353–6.

In some rural areas in which endemic malaria prevails, there is a tendency to regard all cases exhibiting rigor, fever and sweats as cases of malaria, especially in the malaria season. This facile diagnosis may lead to grave errors. Other infections may cause such symptoms : illustrative cases are described. The examination of thick blood smears and, when necessary, a differential white blood cell count, may help to avoid errors. On the other hand, malarial infections may simulate other diseases. In the Extremadura Province of Spain, dysenteric forms of *P. falciparum* infections are not rare. *Norman White.*

PAMPANA. La malaria nella ex-Jugoslavia. Studio Riassuntivo. [**Malaria in Jugoslavia.**] *Riv. di Malariologia.* Sez. I. 1941, Mar.–June, v. 20, Nos. 2/3, 205–26, 7 figs. & 1 map. [21 refs.] German summary (4 lines).

CASINI, G. Notizie e rilievi sull'epidemiologia della malaria in Albania fino a 1939–40. [**The Aftermath of the Malaria Epidemic in Albania, 1939–40.**] *Riv. di Malariologia.* Sez. I. 1941, Mar.–June, v. 20, Nos. 2/3, 75–115, 11 maps. German summary.

FITZGERALD, P. J. **Malaria at a Caribbean Base.** *U.S. Nav. Med. Bull.* 1946, July, v. 46, No. 7, 1140–52, 2 figs. [17 refs.]

This report describes malaria incidence in the U.S. Naval Station at Guantanamo Bay, Cuba. Guantanamo Bay is on the southern shore of the eastern tip of Cuba in Oriente Province. A malaria survey of Oriente Province was made by CARR and his colleagues [this *Bulletin*, 1940, v. 37, 664] and BROWN and WARE's observations on mosquito and malaria control in the Caribbean Area [this *Bulletin*, 1942, v. 39, 436] were made at Guantanamo. The United States has maintained a permanent naval station there since 1903. Large scale constructional work in 1940–41 led to an exacerbation of the previously very mild endemic malaria ; imported labour introduced new strains of infection and man's activities increased the breeding facilities for *A. albimanus*, the local vector. Mosquito control measures begun in 1943 averted a large outbreak. In 1945 there were 141 service and 52 civilian cases of malaria recorded, the highest incidence recorded in 16 years ; most of the patients had visited the

nearby cities of Guantanamo and Santiago de Cuba and probably acquired infection there. Rainfall was light in 1945 and very few anophelines were found in the Guantanamo Base.

P. falciparum infections were three times more numerous than *P. vivax*. Among 381 malaria cases there were 16 *P. malariae* infections, four of which were possibly acquired locally. Clinically malaria at Guantanamo Bay is of a mild type. *Norman White.*

Woodhill, A. R. & Lee, D. J. **The Subspecies of *Anopheles amictus* Edwards (Diptera, Culicidae).** Reprinted from *Proc. Linnean Soc. New South Wales*. 1944, v. 69, Pts. 1–2, 62–6, 8 figs.

By the breeding of series from isolated females the authors have shown that there are two forms of *Anopheles amictus*, the type form *A. amictus amictus* and the " Hill's variety " which they name *A. amictus hilli*. The type form occurs from the northern part of Western Australia across northern Australia and in the eastern part of Queensland to the New South Wales border. *A. amictus hilli* occurs in the above areas but also in Dutch New Guinea ; older records from Dutch New Guinea undoubtedly refer to the subspecies *hilli*. Some additional characters for the identification of the type form are given and for *hilli* the female, male, larva and egg are described in full and the chief morphological details are figured. *H. S. Leeson.*

Woodhill, A. R. & Lee, D. J. **Some New Records and New Synonymy of Australian Species of *Anopheles* (Diptera, Culicidae).** Reprinted from *Proc. Linnean Soc. New South Wales*. 1944, v. 69, Pts. 1–2, 67–72.

The distribution is recorded of *Anopheles meraukensis* Venhuis and *A. novaguinensis* Venhuis on the mainland of Australia. Both species were originally described from Dutch New Guinea, the latter as *Anopheles punctulatus* var. *novaguinensis* which the authors now raise to specific rank. They also establish new synonymy for *Anopheles annulipes* Walker and *A. novaguinensis* Venhuis. The original descriptions were in Dutch and are here presented fully translated into English. *H. S. Leeson.*

Young, M. D., Stubbs, T. H., Ellis, J. M., Burgess, R. W. & Eyles, D. E. **Studies on Imported Malarias. 4. The Infectivity of Malarias of Foreign Origin to Anophelines of the Southern United States.** *Amer. J. Hyg.* 1946, May, v. 43, No. 3, 326–41, 1 fig.

Previous reports have described the methods used in these studies [this *Bulletin*, 1946, v. 43, 5]. The present observations were carried out in laboratories in Texas, North Carolina and South Carolina. Mosquitoes in lots of 100 or more were fed upon patients with relapsing malaria acquired overseas. After feeding the mosquitoes were placed in an insectary with a temperature between 74 and 80°F. and high relative humidity. More than a million mosquitoes were handled :—982,613 *A. quadrimaculatus*, 3,170 *A. punctipennis*, 1,075 *A. pseudopunctipennis pseudopunctipennis*, 3,731 *A. walkeri*, and 13,014 *A. albimanus*. The origins of the infections were :—South Pacific 117, Mediterranean 40, Caribbean 6, Liberia 1, Burma 1. There were 2 *P. falciparum* infections ; the remainder *P. vivax*. Sixty-one per cent. of the patients infected mosquitoes : the infection rate of 6,247 mosquitoes dissected was 30·8 per cent. *A. quadrimaculatus* transmitted infections to neurosyphilitic patients.

The average gametocyte count in the relapses was 3·4 per 100 white cells. The patient who had had most relapses, 24, and the patient with the longest

duration of the disease, 31 months, both infected mosquitoes. The average length of the sporogonous cycle of *P. vivax* in *A. quadrimaculatus* was 10·7 days ; the shortest 8 days.

A numerical evaluation of the relative susceptibility to infection of four species of *Anopheles* was :—*A. punctipennis* 100 ; *A. quadrimaculatus* 98 ; *A. pseudopunctipennis pseudopunctipennis* 40 ; *A. albimanus* 2. Too few *A. walkeri* were dissected to justify comparison. *Norman White.*

Lifschitz, J., Umana, A. C. & Vergara, J. J. Hallazgo de *Anopheles* (*N*) *darlingi* Root con ooquistes. (Nota previa.) [**Presence of** *Anopheles* (*N*) *darlingi* **in some Argentine Ports.**] *An. Inst. Med. Regional.* Tucumán, Argentine. 1946, Aug., v. 1, No. 3, 349–55, 1 map. [Summary in English by the author.]

" (1) We found as a possible vector in the zones of Port Iguazú, Iguazú-Cué (Port Aguirre), Port Benberg and Port Eldorado, the *Anopheles* (*N*) *darlingi* Root, during the malarial epidemic we had in February–March, 1946.

" (2) In 260 dissections of *Anopheles* (*N*) *darlingi*, caught full of blood in houses, we found 5 stomachs with young oöcysts, the proportion obtained being 1·92 per cent."

Hackett, L. W. **The Malaria of the Andean Region of South America.** *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 239–52. [13 refs.]

Anopheles pseudopunctipennis is responsible for a great amount of malaria on both slopes of the Andes from northern Argentina to Colombia. It breeds in unshaded pools of clean fresh water containing green algae, along the margins or in the beds of hill streams and is thus specially adapted to mountainous regions with a long dry season. It is responsible for endemic malaria at heights ranging from 250 to 2,500 metres above sea-level. Cold in Argentina and increasing dryness in Chile determine the southern limits of its prevalence, 31°S. in Argentina, 20°30′ S. in Chile. The upper limit of its breeding is not a fixed point in any valley ; it varies from year to year. Water temperature is probably the limiting factor. It is probably the highest malaria vector in the world ; it is responsible for malaria in the Cinti Valley of Bolivia above the town of Camargo, where the Quebrada de Tota is above 2,600 metres throughout its entire length.

A. pseudopunctipennis breeds in an uninterrupted belt on both slopes of the mountain range from Argentina to New Mexico, but between Ecuador and Guatemala and again north of the Valley of Mexico it loses much or all of its capacity to transmit malaria. It is probably not a homogeneous species but consists of two or more varieties as does *A. maculipennis* in Europe.

Norman White.

Castillo, R. L. Une revue des anophèles de l'équateur. [**A Survey of the Anopheles of Ecuador.**] *Rev. Paludisme et Méd. Trop.* 1946, Oct. 15, v. 4, No. 29, 237–8.

The author lists the species of Anopheles of Ecuador which he has encountered on expeditions during the last four years. He arranges them into three groups corresponding to the geographical regions of the country and notes their importance in relation to malaria.

Along the Pacific coast *Anopheles albimanus* is the chief vector (3–15 per cent. infected), *A. punctimacula*, though a vector in Panama and Colombia, was not found infected in Ecuador. *A. aquasalis* is suspected, but not proved,

to be a vector. *Chagasia bathanus, Anopheles eiseni, A. pseudopunctipennis levicastilloi, A. apimacula, A. mediopunctatus, A. neomaculipalpus, A. triannulatus davisi* and *A. neivai* are of no importance.

In the inter-Andean area the most dangerous anopheline is said to be *A. pseudopunctipennis rivadeneirai* ; 5–20 per cent. have been found infected in nature (this is a new member of the *pseudopunctipennis* complex and no figures are given of the number of dissections made). *A. eiseni* and *A. punctimacula* are also found here.

In the Amazon region, east of the Andes the vector is *A. darlingi* ; *A. boliviensis* is suspected and *A. bambusicolis, A. oswaldoi* and *A. kompi* are of no importance. [See also this *Bulletin*, 1946, v. 43, 262.] *H. S. Leeson.*

Arnold, E. H., Simmons, S. W. & Fawcett, Dorothy G. **Precipitin Technique for determining Mosquito Blood Meals.** *Pub. Health Rep.* Wash. 1946, Aug. 23, v. 61, No. 34, 1244–9, 6 figs. (4 on 2 pls.).

The Rice and Barber modification of the Uhlenhuth-Weidanz precipitin test has been used by the authors on over 150,000 mosquitoes including *Anopheles quadrimaculatus, A. pseudopunctipennis, A. albimanus, A. punctipennis, A. crucians, A. freeborni*, and *A. punctulatus.*

The method is described and illustrated by photographs [see this *Bulletin*, 1935, v. 32, 807] ; a sample "daily work sheet" and a "host and habitation summary sheet" are shown. No results are given. *H. S. Leeson.*

Perves, M. Observations de paludisme héréditaire et congénital. Paludisme du nourrisson. [**Hereditary and Congenital Malaria and Malaria of Infancy.**] *Rev. Paludisme et Méd. Trop.* 1946, Feb. 15, v. 4, No. 23, 33–6.

——. Transmissions héréditaire et congénitale du paludisme à *Pl. falciparum.* Influence de la maladie sur les premiers mois de la vie. [**Hereditary and Congenital Transmission of *P. falciparum* Malaria : Influence of the Disease on the Early Months of Life.**] *Ibid.* July 15–Sept. 15, No. 28, 193–203, 1 chart.

On the upper reaches of the Nyong in the French Cameroons is a swampy forest area where trypanosomiasis, malaria and leprosy have long flourished. To alleviate the conditions, the administration of this Upper Nyong region was entrusted to a group of doctors. It is here that the observations recorded were carried out.

Autopsies were made on four stillborn infants. In the spleens of three of them, schizonts of *P. falciparum* were found ; in one spleen a rosette and two macrogametes were also seen.

In the maternity clinic at Abong M'Bang blood smears from finger and umbilical cord, of both mothers and infants, are examined. Among 661 infants and 651 mothers, 50 per cent. of the mothers and 10 per cent. of the infants harboured parasites. These were all *P. falciparum* infections, except 3 maternal *P. vivax* infections. *P. falciparum* gametes were found in 25 mothers and in 8 infants. Congenital infections are thus by no means rare, but clinical manifestations of malaria have not been seen by the author during the first two months of an infant's life. From then onward, clinical malaria becomes increasingly prevalent. From the end of the fifth to the eighteenth month spleen and parasite rates oscillate between 35 and 45 per cent. Thereafter the rates decline. Troubles of dentition appear to determine and to aggravate malaria attacks. The two most common forms of malaria attacks in infants are gastro-intestinal and pulmonary ; the first clinical manifestation is

frequently dysenteric. Twenty-five per cent. of infants born alive die during the first two years of life: pulmonary affections and malaria are responsible for most of this mortality. *Norman White.*

COGGESHALL, L. T. **Certain Experiences with Malaria during World War II.** *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 229–37.

This paper describes the importance of malaria as a military medical problem during the late war and ably covers familiar ground. The success achieved by mepacrine as a suppressive is acclaimed:—when the plasma level was maintained at 20 gamma or more, almost perfect protection against clinical malaria was obtained. The tenacious character of *P. vivax* malaria acquired in the South Pacific is illustrated, in spite of which enlarged livers and spleens were not common, even in patients who had suffered many relapses. Among 1,424 men examined during their symptom-free period, only 3 per cent. had palpable spleens and only one per cent. had palpable livers. The men had, also, a high degree of physical fitness. During symptom-free periods parasites were found in 8·1 per cent. of blood examinations (4,853 smears examined). The most common complication noted between clinical attacks was headache. On the whole, malaria during the war was a great deal more troublesome than had been anticipated but less fatal. *Norman White.*

JENNINGS, G. H. **Cerebral Malaria in Britain.** [Correspondence.] *Brit. Med. J.* 1946, Dec. 7, 875.

Report of a further case.

DŁUGOSZ, H. **A Case of Blackwater Fever observed in Britain.** *Edinburgh Med. J.* 1946, Aug., v. 53, No. 8, 450–57, 2 figs.

This is a report of a case in which acute haemolysis occurred accompanied by haemoglobinuria. After recovery, benign tertian parasites were discovered in the peripheral blood. The patient had been in the Middle East for two years but had been in England for the six months previous to the onset of haemolysis. While abroad he had taken quinine irregularly.

[There is no clear reason why the author considers this case to be blackwater fever. It might equally well have been Lederer's anaemia. A list of references is given at the end of the paper, but the authors quoted are not referred to in the text.] *B. G. Maegraith.*

TORODE, K. R. **Spontaneous Rupture of the Spleen during a Malarial Rigor.** *Med. J. Australia.* 1946, Sept. 21, v. 2, No. 12, 414–15.

This is an account of a patient who was admitted to hospital by ambulance at night with a provisional diagnosis of malaria, but without a history of it. He had suffered from severe dysentery in the Tropics, and had ceased taking suppressive "atebrin" six weeks previously.

The patient had a temperature of 101°F. and slight epigastric and left hypochondriac tenderness; his spleen was thought to be palpable. In view of the negative history and the absence of proof of malaria, the patient was put under observation. On the next day and the succeeding morning he was symptom-free and walked to the bathroom; at midday he felt nauseated and

had a mild rigor. "A blood smear was examined, with a positive result" [nature of result not stated]. That afternoon at 2 o'clock 10 grains of quinine were given orally; half an hour later the patient developed signs of shock, later complaining of pain over the renal angle, and exhibiting a lax abdomen and splenic tenderness. Treatment with intravenous serum and, later, by repeated blood transfusions, was given: in the interval the patient collapsed completely and by 4 p.m. he was comatose and almost pulseless. Further blood transfusions, "Coramine", adrenalin, and serum were given, and whilst preparations were being made for continuing the blood transfusions the patient died, at 8.30 p.m.

At post-mortem, pints of blood clot and serum were found in the peritoneal cavity. The spleen measured about 12 in. by 6 in. by 4 in. and weighed approximately four pounds; a rupture covering an area of about 6 square inches was present on its postero-inferior surface.

The author records this case as one with which any practitioner may be faced; and he discusses the differential diagnosis, the possibility of surgical intervention and the question of whether the immediate administration of quinine from the time of the patient's admission would have altered the outcome.

[The writer states "In accordance with the usual routine treatment in an unproven case of malaria, and indeed in view of the largely negative history, the patient was placed under observation." It is not clear why, "with a provisional diagnosis of malaria", there is no record of blood films having been examined on the patient's admission to hospital, or indeed until he developed a rigor in the middle of the third day.] *H. J. O'D. Burke-Gaffney.*

Matilla, V., Covaleda, J. & Aparicio Garrido, J. El estado inmunitario de los indigenas "bubis" de Fernando Poo frente a la infección paludica. Estudio de su esplenomegalia. [**State of Immunity against Malaria of the Bubi Tribe of Natives of Fernando Po. Study of their Splenomegaly.**] *Med. Colonial.* Madrid. 1946, Apr. 1, v. 7, No. 4, 309–17, 1 chart. [12 refs.]

The Bubis are the dominant native race of the isle of Fernando Po. The authors examined 587 young people of the race for enlargement of the spleen and record their findings in six age groups:—0–1, 1–3, 3–5, 5–9, 9–14 and 14–20. The global spleen rate was 58·6 per cent. The highest rate was in the 3–5 group, 88·5. The 0–1 rate was 59·5. In the 14–20 group the rate was 35·6. The Ross Index was highest in the 1–3 age group, 2·50; thereafter the size of the spleens decreased. There was no size IV spleen in the 9–14 age group, and no III spleen in the 14–20 group. There was no significant difference between the rates for the two sexes. *Norman White.*

Makari, J. G. **The Cephalin-Cholesterol Flocculation Test in Chronic Malaria and its relation to Endemicity.** *J. Trop. Med. & Hyg.* 1946, Oct.–Nov., v. 49, No. 5, 92–4, 2 figs.

The author refers to a previous paper [this *Bulletin*, 1946, v. 43, 623] concerning the cephalin-cholesterol flocculation test in 105 patients suffering from malaria. There were 92 American refugees at Anjar among them, and he has been able to follow a group of these patients during the early period of high endemicity and subsequently during the period of low endemicity which followed successful mosquito-control measures. The patients, 46 in all, were studied over a 2½-year period, being examined in February 1943, August 1943 and August 1945.

The following data were obtained :—

	First interview February 1943	Second interview August 1943	Third interview August 1945
	Per cent.	Per cent.	Per cent.
Last attack within two months	100	—	20
Positive splenic enlargement	76	60	27
Positive hepatic enlargement	12	55	55
Positive smear for malaria parasites	60	—	0
Positive C.C.F. test	92	91·5	52

The author notes the fall in the C.C.F. rate, the spleen rate and the parasite incidence, with the drop in endemicity. Tables are given which show correlation coefficients : there was a moderate correlation between the C.C.F. test and the liver and splenic enlargements, and a very high negative one between that test and the duration of malarial infection—the shorter the infection, the stronger the test. There was also a fairly high positive correlation between the C.C.F. test and the last chill in months. On the analogy of the behaviour of foreign proteins—which, according to JAFFE cause a swelling, proliferation and mobilization of the reticulo-endothelial cells on injection—the author suggests that the sudden liberation of burst parasites into the plasma, as indicated by a chill, also stimulates the reticulo-endothelial system.

The author quotes the views of SICAULT and MESSERLIN [this *Bulletin*, 1940, v. 37, 862] on malaria as a disease of the reticulo-endothelial system ; and concludes that " it would seem that the longer the stimulation of the malaria parasites to the reticulo-endothelial system, the longer the time required for the system to go back to normal."

In this proposition, he finds an explanation for the persistence of a fairly high C.C.F. rate and hepatic enlargement in his group of patients, even after the marked reduction in endemicity. *H. J. O'D. Burke-Gaffney.*

BECKER, F. T., KAPLAN, L. I. & READ, H. S., in collaboration with M. F. BOYD. **Variations in Susceptibility to Therapeutic Malaria.** *Amer. J. Med. Sci.* 1946, June, v. 211, No. 6, 680–85, 4 figs.

Malaria therapy was used in the treatment of 225 white and 75 Negro soldiers suffering from various types of neurosyphilis. From the experience thus gained certain conclusions emerge. Negroes should be inoculated with *P. malariae* ; they are commonly refractory to *P. vivax* infection. For white patients with no history of naturally acquired malaria, *P. vivax* infections generally give satisfactory results. Of the white patients in this series so treated 43 came from the south-eastern United States ; 80 per cent. of them were susceptible. Ninety-three per cent. of white patients from other parts of the United States were satisfactorily treated with *P. vivax*. If there be a history of malaria or if the patients come from malarious regions overseas *P. malariae* should be used. If there be a spontaneous remission of a *P. vivax* infection before the patient has had a sufficient febrile reaction, reinoculation with *P. malariae* is advocated if the patient has had 5 paroxysms or less ; if he has experienced more than 5 paroxysms, reinoculation with a heterologous strain of *P. vivax* is recommended.

A daily parasite count is desirable. It permits the early recognition of a " runaway " infection. It has also helped to forecast the immune type of

reaction ; the therapeutically inadequate infection can then be terminated and reinoculation done more promptly than would be possible otherwise. *P. vivax* parasitaemias usually average from 20,000 to 40,000 per cmm. and rarely exceed 50,000. Parasitaemias in *P. malariae* infections rarely attain 20,000 per cmm. The danger line in *P. falciparum* infections is from 100,000 to 200,000 per cmm. *P. falciparum* was only used in 3 cases ; the three patients were immune to both *P. vivax* and *P. malariae.* Three-grain doses of quinine are given hourly as long as the temperature in *P. falciparum* infections exceeds 104°F. or when the parasite count exceeds 100,000 per cmm.

Norman White.

KAPLAN, L. I., READ, H. S. & BECKER, F. T., in collaboration with M. F. BOYD. **Use of Quantitative Parasite Inoculation Doses in** *Plasmodium vivax* **Malaria Therapy.** *Arch. Neurology & Psychiatry.* 1946, July, v. 56, No. 1, 65–73, 4 figs.

It is pointed out that in malarial therapy for general paralysis a period of remittent fever of several days' duration precedes the establishment of the malarial paroxysms, which alone are of therapeutic value. The preliminary febrile period is often accompanied by severe malaise and exhaustion, which debilitates the patient to such a degree that he is unable to support well the therapeutic paroxysms when they occur. With the object of discovering a method of infection which would eliminate this preliminary period, various methods of inoculation were investigated in 265 patients. For intradermal inoculation 0·2 cc. of blood containing between 1 and 2 million parasites was inoculated in four portions of 0·05 cc. into four weals on the forearms. In 26 patients 42·3 per cent. showed no preliminary period, while 76·9 per cent. showed a preliminary period of two days or less. Although from the point of view of elimination of this period this method of inoculation gave the best result, it was found to be unsatisfactory in that 18·8 per cent. of the cases failed to become infected. In the case of intravenous inoculations, it was found that the higher the parasite dose the longer was the preliminary period of remittent fever. When the dose was reduced to one of 1 million parasites the period was eliminated in 35·7 per cent. of the cases and was two days or less in 67·9 per cent.

It is recommended that in the treatment of neurosyphilis the standard procedure be the intravenous inoculation of 1,000,000 *P. vivax* parasites in the case of susceptible white patients. As regards cycles of a tertian character, these were noted in 57·8 per cent. of the cases inoculated intradermally, while in cases inoculated intravenously they were most commonly noted in those receiving the lowest doses. Thus they occurred in 25 per cent. of those receiving 26 to 150 million parasites ; 31 per cent. for doses of 6 to 25 million, 32·1 per cent. for doses of 2 to 5 million and 42 per cent. for doses of 1 million. In 58 cases in which mosquito transmission was practised, the preliminary period was three days or longer in 62·1 per cent., while only 22·4 per cent. showed tertian cycles.

C. M. Wenyon.

WINCKEL, W. F. Trois siècles d'usage du quinquina et de la quinine dans la thérapeutique du paludisme. **Three Centuries of Quinine in the Treatment of Malaria.** *Rev. Paludisme et Méd. Trop.* 1946, Nov. 15–Dec. 15, v. 4, Nos. 30/31, 272–8. [Refs. in footnotes.]

BANG, F. B., HAIRSTON, N. G., MAIER, J. & TRAGER, W. **Studies on Atabrine (Quinacrine) Suppression of Malaria. I. A Consideration of the Individual Failures of Suppression.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 649–61, 7 figs. [13 refs.]

These studies of atebrin (quinacrine, mepacrine) suppression of malaria were made in the S.W. Pacific area from June 1943 till January 1945. The earlier

report of FIELD in 1934 [*Bull. Inst. Med. Res. Federated Malay States*, No. 2] had shown the value of the drug as a suppressant in native populations previously exposed to infection. The more recent work on the pharmacology of atebrin by SHANNON *et al.* [this *Bulletin*, 1945, v. 42, 343] and on methods for its estimation by BRODIE & UDENFRIEND and by MASEN [this *Bulletin*, 1944, v. 41, 453; 1945, v. 42, 8] proved of great help in the present investigations. The view that the value of suppressive treatment can be determined by the resultant plasma levels of the drug has in general been confirmed [MARSHALL & DEARBORN from experimental evidence on *P. lophurae* in ducks (see below p. 292) have, however, recently questioned the validity of this conclusion]. The present experiments were carried out partly with troops after a strenuous campaign, some of whom were heavily infected, and with others under more normal conditions. In agreement with earlier writers, great variation was found to occur in plasma levels of individuals receiving the same dose of drug and on the assumption that a certain level was required for protection it appeared that a daily dose of 0·1 gm. would not invariably protect. Such a dosage, or on the other hand 0·4 to 0·5 gm. twice weekly, was, however, in general regarded as adequate. Clinical malaria developed when the drug was present in inadequate amounts, 30 micrograms per litre of plasma being considered as a satisfactory level. Two-thirds of a group of 152 subjects undergoing suppressive treatment were not protected by plasma concentrations up to 10 micrograms per litre, nor were 23 of the same group protected by over 20 micrograms per litre. There was a considerable overlap between the concentrations in protected and non-protected individuals. The authors believe that "atabrine suppression is mainly a problem of drug administration." *J. D. Fulton.*

FAIRLEY, N. H. **Researches on Paludrine (M. 4888) in Malaria. An Experimental Investigation undertaken by the L.H.Q. Medical Research Unit (A.I.F.), Cairns, Australia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Oct., v. 40, No. 2, 105–53, 16 charts & 2 figs. [13 refs.] Discussion 153–62 [WENYON, C. M.; SINTON, J. A.; DAVEY, D. G.; CHESTERMAN, C. C.; MURGATROYD, F.; STANNUS, H. S.; KING, J. D.; FAIRLEY, N. H. (in reply).].

Following the results obtained with the chemically closely related drugs M.4430 and M.4888 (paludrine) against different species of bird malaria by CURD, DAVEY & ROSE [this *Bulletin*, 1946, v. 43, 400], researches on the therapeutic, suppressive and causal prophylactic properties of paludrine were undertaken by the Medical Research Unit at Cairns, Australia. Healthy volunteers infected with the sporozoites of New Guinea strains of *P. vivax* and *P. falciparum*, as well as troops infected during the S.W. Pacific campaign, were used in these experiments. Their scope has been described [this *Bulletin*, 1946, v. 43, 527], and some further work is now included in the present report. Although the clinical response to treatment was not very rapid, paludrine proved more efficient than any other drug in the radical cure of malignant tertian malaria, by the standard course of 100 mgm. thrice daily for 10 days (total 3·0 gm.). In benign tertian malaria a total dosage of 0·1 to 14·0 gm. was used in treatment. Clinical response to therapy in this infection was not more rapid than with quinine or atebrin, and while radical cure of sporozoite-induced infections was not regularly obtained, relapses were fewer than after treatment with other drugs. In a limited number of cases of quartan malaria, there was a rapid clinical response to paludrine administration but parasites disappeared only slowly from the blood and it was not decided whether radical cure had been effected. In dosage of 100 mgm. daily the drug proved adequate for suppression of *P. vivax* and *P. falciparum* infections. In well-tolerated

doses it acted as a true causal prophylactic in the latter infection and as a partial causal prophylactic in the former. Plasmoquine has similar properties but must be given in doses too large to be tolerated. In a field type of experiment, during which volunteers were repeatedly bitten by mosquitoes infected with *P. vivax* and *P. falciparum* over a period of 62 days while being subjected to strenuous conditions of exercise and cold accompanied by injection of adrenaline and insulin, 100 mgm. of paludrine daily kept the blood free from parasites and all symptoms of malaria were absent. Some time after administration of drug overt *vivax* but not *falciparum* malaria developed. From a careful study, in which the drug was administered at different times relative to the bites of mosquitoes infected with *P. falciparum*, it was concluded that pre-erythrocytic forms of the parasite (not yet demonstrated) were more susceptible to its action than were sporozoites or asexual erythrocytic forms. The important conclusion was reached—" that 50 to 100 mg. administered twice weekly at 3 to 4 days interval, should afford complete causal prophylaxis against *P. falciparum* infections." In view of the ability of paludrine as a schizonticide to bring about clinical cure of malarial attacks in non-immunes, it seems probable that epidemics among native populations could be controlled by a single weekly dose. The factors involved in the treatment of native populations are discussed and the author suggests that, with paludrine available in adequate quantities, the radical cure of native populations is now feasible, for subsequent epidemics could be controlled if they occurred, but he agrees that long-term field investigations are indicated. Paludrine is not gametocidal in the human host, but prevents complete development in the mosquito. It has a powerful action against early schizonts by preventing division of chromatin and merozoite formation. In therapeutic doses, it produces no significant toxic effects, nor were any such effects noted in patients who received a course of 300 mgm. daily for three weeks followed by a dose of 100 mgm. twice weekly over a period of six months. By the latter treatment the number of relapses in *vivax* malaria was greatly reduced. The value of quinine-plasmoquine and paludrine-plasmoquine therapy, regarding the incidence of radical cure in *vivax* infections, is meantime being assessed in large numbers of patients. *J. D. Fulton.*

CURD, F. H. S. & ROSE, F. L. **A Possible Mode of Action of " Paludrine ".** [Correspondence.] *Nature.* 1946, Nov. 16, 707–8.

While seeking an explanation of the mode of action of paludrine it was found that this potent antimalarial formed a copper complex in which one atom of the metal was associated with two molecules of the drug. The construction of space models of this compound indicated several points of resemblance between it and naturally occurring porphyrin pigments. It is suggested that paludrine may exercise its antimalarial action through interference with the porphyrin metabolism or enzyme systems of the parasite. [Many investigations on the respiratory enzymes of malaria parasites have been reviewed (this *Bulletin*, 1938, v. 35, 709 ; 1945, v. 42, 448, 967 ; 1946, v. 43, 824, 825) and while haematin is known to be formed, further studies on porphyrin metabolism have not been reported.] Copper need not necessarily be the metal involved in such processes and provided the structural features of the complex are preserved activity may be shown even in the absence of a metal. Because of the low toxicity of paludrine and its inactivity against many other micro-organisms the authors consider that the suggested antagonism must relate to a highly specific porphyrin system in the malaria parasite.

J. D. Fulton.

JOHNSTONE, R. D. C. **Relapsing Benign Tertian Malaria treated with Paludrine.** *Lancet.* 1946, Dec. 7, 825–6.

The following three different courses of treatment were carried out in rotation:–
(1) Paludrine 0·05 gm. daily for ten days.
(2) Paludrine 0·5 gm. daily for ten days.
(3) Quinine gr. 30, pamaquin 0·03 gm. daily for ten days.

Those who had received any treatment before admission to hospital were excluded, but in every case there was a previous history of malaria.

Between July 1945 and March 1946, 324 or 108 cases of each series were thus treated.

When the patients arrived in the ward, blood slides, both thin and thick, were taken and treatment instituted on those showing *Plasmodium vivax*. The drugs were administered in divided doses—paludrine twice daily, the quinine-pamaquin three times daily after food. None of the paludrine-treated cases exhibited any digestive symptoms. Patients were confined to bed until they were afebrile for 48 hours.

In the first 240 cases, blood films were examined on the 8th, 9th and 10th days of treatment. The results of these investigations were negative for asexual parasites, with the exception of one patient on quinine-pamaquin who showed scanty B.T. rings on the 9th day. Subsequently he remained free from relapse after six months. There was rapid response to all forms of treatment and little difference could be detected in results. The length of pyrexia after the start of treatment was :—

Paludrine (0·05 gm.)	1·49 days
,, (0·5 gm.)	1·47 ,,
Quinine-pamaquin	0·98 ,,

The *remote response* was obtained by the issue of a standard form requesting information regarding further relapses. Every patient has been followed up, with one exception. The results are shown below :—

TABLE 1.—*Remote results of treatment.*

Course	No. of cases	Free from relapses	One proved relapse	Two or more proved relapses	Clinical relapse	Percent. relapsed	
						All cases	Proved cases
Paludrine (0·05 gm.)	108	62	26	7	13	42·6	30·5
Paludrine (0·5 gm.)	107	60	23	2	22	43·9	23·3
Quinine-pamaquin	108	91	9	1	7	15·6	9·2

The quinine-pamaquin results obtained have been compared with a former series which showed relapse-rates of 10·3 per cent. proved cases and 16·5 per cent. total relapses. There is, therefore, no significant difference in the quinine-pamaquin results ; and those obtained with paludrine may be concluded to be approximately accurate.

In the total series, 89 (27·4 per cent.) were ex-prisoners of war from the Far East and these have been separately analysed. Owing to their privations, the relapse-rate was higher than in other cases. They have, however, been included in the totals, though it is realized that the total relapse-rate has been increased.

The *time interval* between arrival in England and admission to hospital was compared :—

	Average months in U.K.	Maximum
Paludrine (0·05 gm.)	3·26	11 months
,, (0·5 gm.)	3·31	1 year
Quinine-pamaquin	3·13	9 months

Different strains of *P. vivax* may possibly cause relapses at different intervals :—

	India-Burma	Mediterranean	Far East	Others
Paludrine (average for both courses)	65·5	10·5	30	1·5
Quinine-pamaquin	64	14	29	1·0

Thus the *area of infection* does not seem to influence the relapse-rate.

The interval between treatment and proved relapse is assessed as follows :—

	Average number of days between treatment and relapse
Paludrine (0·05 gm.) ...	65·1
,, (0·5 gm.) ...	53·0
Quinine-pamaquin ...	43·7

These figures have been vitiated to some extent by the practice of some who took occasional courses of mepacrine after leaving hospital, with the result that the relapse period might thereby have been prolonged.

P. Manson-Bahr.

DE OLIVEIRA, A. Novo medicamento quimoterápico antimalárico. [**New Chemo-Therapeutic Medicament against Malaria.**] *Rev. Brasileira Med.* Rio de Janeiro. 1946, Aug., v. 3, No. 8, 626–9. [13 refs.] [Summary in English by the author.]

"After examining the properties of a number of compounds employed in malaria treatment and prophylaxis, the author studies a new synthetic, the chloro-diethyl-aminomethyl-butylamin-quinolein biphosphate, so-called "W-7618", known in the market under the name of *Aralen*, and on which he comes to the following conclusions :—

"(I) in benign tertian as well as in quartan, the new medicament proved to be 3 times more active than Mepacrine, both as suppressing and curing agent ;

"(II) in malign tertian the therapeutic power is complete, suppressing the attack and extinguishing the infection ;

"(III) it does not, like acridinic substances, cause yellowish pigmentation of the epithelial tissue."

SWELLENGREBEL, N. H. **Malaria Control in the Netherlands.** *Chemical Products.* 1946, Sept.–Oct., v. 9, Nos. 11/12, 98–102.

Benign tertian (*Plasmodium vivax*) is practically the only form of malaria endemic in the Netherlands ; the subject is dealt with in detail in the book "Malaria in the Netherlands" by N. H. Swellengrebel and A. de Buck, 1938,

Amsterdam, Scheltema and Holkema. In the present paper, the author discusses how control of malaria in the Netherlands may be affected by certain recent events—the discovery of " paludrine " and DDT and the destruction of large numbers of domestic animals during the German occupation of the country.

The mosquito vector is the " shortwing " (*atroparvus*) variety of *Anopheles maculipennis* ; it prefers to breed in brackish water and malaria is therefore mainly limited to the coastal provinces called Friesland, North-Holland, and Walcheren Island in Zeeland. The mosquitoes feed and lay eggs during the spring and summer, ceasing to lay eggs usually in August but continuing to feed till the end of October or later ; egg-laying having ceased, they remain in animal and human houses and can infect people until well into December.

Another variety of *A. maculipennis* called " longwing " (*messeae*) which prefers to breed in fresh water and ceases to feed and to lay eggs at the same time, has been regarded as negligible as a malaria vector though it can transmit the infection ; with the destruction of many domestic animals, however, it may feed more on man and may spread malaria to places hitherto free.

The Dutch strains of *P. vivax* have a long (7 to 9 months) incubation period in most infected persons ; infection takes place chiefly in the autumn, after the egg-laying period, and fever appears in the spring and summer of the following year, a circumstance that has an important bearing on control.

Spraying of selected houses has been done with pyrethrum extracts fortnightly from August 15 to the end of September or later, involving four or five sprayings ; it is costly and some infected houses might be omitted, so it is now proposed to spray all the houses once with the more persistent DDT in August (or twice if October should be very mild). During the egg-laying season, the risk of infected mosquitoes returning to human dwellings and infecting other people is kept low by the counter-attraction of animal houses—" stabular deviation " ; with the destruction of animals, the increased risk can be met by an additional spraying with DDT early in July.

There are many so-called healthy or presumptive carriers of *P. vivax* who naturally object to taking 15-grain doses of quinine twice a week ; it is thought that " paludrine ", taken once a week to sterilize the blood, will be more acceptable and more successful as a control measure. *J. F. Corson.*

SWELLENGREBEL, N. H. & KRAAN, H. 10 jaar spuitcampagnes tegen malaria. [**Ten Years of House Spraying against Malaria.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1946, Oct. 12, v. 90, No. 41, 1377–80, 2 graphs. [Summary in English by the authors.]

" A ten years' observation on the effect of house spraying, with pyrethrum solutions, during the transmission period of malaria (August–October). Malaria was greatly reduced in rural areas ; they even withstood the onslaught of the severe epidemic which started in 1944. In urban areas the results were unsatisfactory."

VINCKE, I., with the collaboration of M. LIPS & R. CAMBIER. Note sur l'effet du D.D.T. sur *Anopheles funestus* Giles. [**Note on the Effect of DDT on *A. funestus* Giles.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 175–84, 1 chart.

Since February 1946, experiments with DDT have been conducted against *Anopheles funestus* in a camp near Elizabethville, Belgian Congo. Large breeding places of this anopheline are nearby and the adult density has been under observation since May 1944. Figures are given to show that there is

considerable variation in the numbers of *A. funestus* frequenting different houses and also in the size of the blood-meal contained in the stomachs of captured females.

Four huts were selected and sprayed with different doses of 5 per cent. DDT in kerosene ; controls were established and other huts were sprayed with pyrethrum. Examination of the *A. funestus* taken from the treated huts shows that DDT does not prevent the mosquitoes feeding ; for example, in a collection of 26 *A. funestus*, 19 contained fresh blood, 12 of them with stomachs more than three-quarters full. The numbers of living anopheles collected from the DDT-treated houses remained low for at least two months but increased in huts sprayed with pyrethrum, indicating that the latter insecticide possessed some initial repellent effect which gradually diminished.

The occurrence of living mosquitoes in treated houses does not necessarily mean that the DDT is ineffective, for the mosquitoes might have died later. It is also pointed out that mosquitoes already irritated by DDT in one house may enter other houses and die there.

These experiments are regarded as preliminary and not entirely conclusive, but so far as they go the authors believe that they demonstrate that DDT is slow in action ; that its toxic effect is lasting ; that it has no repellent effect and that it cannot be used for personal protection. It is hoped to use DDT on a large scale against adult anophelines in parts of the town where the densities are highest and where breeding places are difficult to control. *H. S. Leeson.*

TRAPIDO, H. **The Residual Spraying of Dwellings with DDT in the Control of Malaria Transmission in Panama, with special reference to** *Anopheles albimanus*. *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 383–415, 13 figs. on 3 pls. & 2 charts. [24 refs.]

In the summer of 1944, a field experiment was set up in the middle Chagres River, Panama, to study the effectiveness of DDT residual spray treatment of native dwellings in the control of malaria vectors and malaria. The area was one in which intensive studies of malaria and anopheles have been carried on by Dr. H. C. Clark and his associates at the Gorgas Memorial Laboratory during the past fifteen years.

The principal vector of malaria is considered to be *Anopheles albimanus* ; this species [in contrast to *Anopheles gambiae*] does not rest in dwellings during the daylight hours. The principal breeding places are extensive dense mats of *Najas arguta* on the surface of the numerous backwaters and lagoons artificially created with the formation of Gatun Lake during the construction of the Panama Canal.

The three villages studied were accessible only by dugout canoe or foot trail ; malaria rates based on thick blood film examinations were available on a monthly basis for ten years and on a bi-monthly basis for the last five years ; one village was chosen for treatment, the other two being used as controls. Continuous and abundant production of malaria vector species occurred throughout the year. Trained native helpers and collectors were available.

The native houses are typical of the tropics with palm thatch roofs and walls of cane or board.

Mosquito population was assessed by hand catching methods at night between the hours 6.30 and 9 p.m. and 5.30 and 6.30 a.m. ; mosquitoes were conveyed to the laboratory in suitable cages for examination, counting and estimation of survival times. Horse-baited stable traps were found to give a reliable index of outdoor mosquito activity.

Five per cent. DDT in kerosene was applied by pressure sprayers which were regular items of Army issue ; a uniform rate of application was obtained by training spray operators to wet surfaces without permitting the solution to run. The interior of houses was comprehensively treated from ceilings or roof to floor and included furniture surfaces which might be used as resting places by mosquitoes. The exterior surfaces of walls and the undersides of overhanging eaves were sprayed. All outhouses and animal shelters were treated inside and outside. It was difficult to estimate quantities used but the average was approximately three gallons of solution per house. Second and third applications were made at intervals of four months.

Results :—The period covered is from October 1st, 1944, to December 23, 1945.

(1) Mosquito population. There was an immediate dramatic drop in the numbers of anopheles in the treated village after the first treatment from 140 to below 10 anopheles per house per night ; this gross reduction was maintained and reduced to practically nil after the third spraying, about July 1st, 1945 ; a progressive slight increase followed and in the absence of a fourth spraying the anopheline density reached 7 per house per night. The concurrent variations (associated with season and rainfall) in anopheline population in the untreated control villages are also given in statistical tables and the whole illustrated by chart.

(2) Mosquito engorgement. A marked and consistent difference between the percentage engorged in the control and treated villages was found, 27·4 per cent. to 74·3 per cent. in control villages and 0·0 per cent. to 16·7 per cent. in the treated village. Only at the end of the study period, that is six months after the third spraying, did the percentage engorged in the treated village approximate that at the control villages.

(3) Mosquito survival. Of engorged anophelines 4·2 per cent. in the treated village survived twenty-four hours as compared to 38·3 per cent. in the control villages. No significant difference between control and treated houses was evident six months after the third spraying.

It is indicated that DDT treatment tends selectively to reduce the malaria transmission potential by affecting principally those mosquitoes concerned in transmission ; with each successive treatment the degree of control improves, after the third spraying the malaria transmission potential being reduced 99·9 per cent.

(4) Statistics are given of stable trap catches which give an indication of the anopheline population outside the houses. The following tentative generalizations are made :—

(*a*) At times of great anopheline abundance a high degree of area control may be effected for two or three weeks by spraying of houses alone.

(*b*) During a period of moderate anopheline abundance, effective control for six weeks following house spraying may result.

(*c*) House spraying three months prior to a period of great anopheline abundance is wholly ineffective in preventing the normal increase of Anophelines in an area.

(*d*) The effects of spraying houses as indicated above may extend outwards some three hundred feet but no " peripheral " effect on anopheline population is evident at a distance of 900 feet.

(5) Malaria incidence. The comparison of the malaria rates at the three villages appears in the following table and is based on the cumulative rate in individuals examined either five or six times during the year by the thick blood film method.

	Villages 1 and 2	Village 3	Difference
	Per cent.	Per cent.	Per cent.
[1]1940–41	45·6	33·3	−12·3
[1]1941–42	52·8	60·9	+ 8·1
[1]1942–43	39·7	46·7	+ 7·0
[1]1943–44	42·5	45·5	+ 3·0

	First Spraying November 1st, 1944		
	Untreated Per cent.	Treated Per cent.	Per cent.
[2]1944–45	51·3	24·0	−27·3
[3]1945	52·0	14·8	−37·2

[1]Annual rate based on the year September to August. [2]Annual rate based on the year November to October. [3]Annual rate based on the year January to December.

[This paper requires to be studied in the original by the hygienist, whose responsibility it is to apply the "residual insecticide" method of malaria control.] *R. Ford Tredre.*

Deonier, C. C., Jones, H. A. & Incho, H. H. **Organic Compounds effective against Larvae of** *Anopheles quadrimaculatus*—**Laboratory Tests.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 459–62.

"Of the 6,000 organic compounds tested to determine their toxicity to fourth-instar larvae of *Anopheles quadrimaculatus* Say only 175 gave mortalities of over 50 per cent. in 58 hours at 1 p.p.m. Twenty-two compounds, in addition to DDT and related compounds, showed toxicity at 0·1 p.p.m. Acetic acid, 1-trichloromethyl-2,2,-methylene bis (4,6-dichlorophenyl) diester, benzene hexachloride, and *Synthetic 3856* were superior to the other compounds in their toxicity to anopheline larvae."

Richardson, A. P., Hewitt, R. I., Seager, L. D., Brooke, M. M., Martin, F. & Maddux, H. **Chemotherapy of** *Plasmodium knowlesi* **Infections in** *Macaca mulatta* **Monkeys.** *J. Pharm. & Exper. Therap.* 1946, July, v. 87, No. 3, 203–13, 3 figs. [13 refs.]

The authors are critical of techniques employed in the past for evaluating the effect of drugs on *P. knowlesi* infections in *Macaca mulatta* (*Macacus rhesus*) monkeys because of lack of standardization of the infecting inocula, as well as of dosage, time and rate of administration of drugs under test. They have used the intravenous route of inoculation and in chemotherapeutic tests gave 50 million parasitized cells per kilogram of body weight. On the day after inoculation in untreated animals, scanty parasites were generally detectable in the peripheral blood and on the 5th or 6th day 30 to 90 per cent. of the red cells were infected, and death of the host usually occurred on the 6th or 7th day after infection. In a series of 46 control animals so infected, four survived to become chronic—an unusually large proportion in this infection. By the 7th day 80·2 per cent. of the animals had died and those which survived for 11 days

remained alive indefinitely. The average day of death for the others was 6·3±0·71. Most of the animals reached a peak of infection by the sixth day and all of them before the tenth day. Three criteria were selected as an indication of the efficacy of drugs used in treatment, namely, the percentage mortality, the day of death, and highest parasite count up to and including the tenth day after infection. In the chemotherapeutic tests, the standard inoculum was prepared from an infected animal with 20 to 50 per cent. of the red cells infected, and each test animal was housed individually and received liberal diet. Blood counts were made at the same time daily. Drugs were given by stomach-tube in a volume of 10 cc. per animal at each dose 18 hours after inoculation; administration was continued for 5 days. To maintain a constant level of drug in the blood the daily dose was divided into three equal parts and given at 8-hour intervals. As already recorded [this *Bulletin*, 1934, v. 31, 172, 700; 1935, v. 32, 116, 787] quinine is not an effective drug in this infection and the present authors reached the same conclusion. It was shown by COGGESHALL [this *Bulletin*, 1939, v. 36, 824] that various sulphonamides were very active in *P. knowlesi* infections and that they could effect radical cure. The range of antimalarial activity of sulphadiazine has now been investigated; and on the basis of oral dosage is regarded as 175 times as effective as quinine, since doses of 0·12 mgm. per kilo, had an effect on the course of the disease comparable with that of 22·2 mgm. quinine alkaloid for the same weight. Sterilization was effected by 0·24 mgm. per kilo. of sulphadiazine. The effective dose was so small that it could not be correlated with blood-levels of the drug. It was antagonized by *p*-aminobenzoic acid. By delaying the start of treatment with quinine and sulphadiazine until 72 hours after inoculation, when the infection has become well established, it was found that both drugs acted at the same rate, and that the effective dose of each was approximately the same as when treatment was begun 15 hours after inoculation. *J. D. Fulton.*

HAAS, V. H., WILCOX, Aimee, DAVIS, Frances P. & EWING, Frances M. *Plasmodium gallinaceum* **Infection characterized by Predominance of Exo-Erythrocytic Forms.** *Pub. Health Rep.* Wash. 1946, June 21, v. 61, No. 25, 921–8.

Working with a strain of *P. gallinaceum*, the authors have noted that if sporozoite infection is carried out after a number of blood passages have been made, the resulting infection is liable to be of the exoerythrocytic type, in which death of the chicks from the presence of large numbers of exoerythrocytic forms in the brain occurs either before any erythrocytic parasites appear in the blood or when these are few in number. When a second serial sporozoite passage was made the same type of infection occurred, but with the third serial sporozoite passage this type of infection ceased to develop almost entirely, only a very small percentage of chicks showing the exoerythrocytic type of infection. In all subsequent serial sporozoite passages the infection was of the erythrocytic type which follows blood inoculation, in which there develops a heavy blood infection concurrently with the appearance of exoerythrocytic forms in the brain and leptomeninges. The same results were obtained when sporozoite infections were carried out after serial blood passages had been made for still longer periods. As is well known, chicks subjected to blood inoculations were found to have exoerythrocytic forms in the brain after subsidence of the erythrocytic infection. Emulsions made from the brain at this time were inoculated into chicks subcutaneously. The infections which developed were of the exoerythrocytic type, with few or no parasites in the blood. Emulsions

of the brains of these chicks were inoculated to others. With each passage a decreasing number of chicks became infected, till, at the sixth, none became infected. Brain emulsions were also inoculated into the embryonic yolk of 7- to 9-day old embryos. The resulting infections, proving fatal in a few days, were of the exoerythrocytic type. Brains of these embryos were used for serial passages, which so far have been successful up to the fourth passage with the same type of infection. The authors suggest that the type of investigation carried out by them may be useful in the search for exoerythrocytic stages of development of mammalian malarial parasites. *C. M. Wenyon.*

Brackett, S., Waletzky, E. & Baker, Margaret. **The Relation between Pantothenic Acid and *Plasmodium gallinaceum* Infections in the Chicken and the Antimalarial Activity of Analogues of Pantothenic Acid.** *J. Parasitology.* 1946, Oct., v. 32, No. 5, 453–62. [16 refs.]

A guide to the synthesis of new antimalarials has been sought by studying the pantothenic acid requirements of *P. gallinaceum* in chicken hosts. Some of its analogues are known to possess chemotherapeutic activity in other infections and a number of these synthetic substances were tested for antimalarial activity. The *in vivo* method of approach was used because of the lack of a suitable method for *in vitro* cultivation of the parasite and also for the reason that the pantothenate requirements of the host were already well known. Attempts to correlate the intensity of a malarial infection in a particular host with dietary deficiencies have given somewhat conflicting results. In the present experiments, chickens were rendered pantothenate-deficient by feeding them, from the time of hatching, on a special diet in which pantothenate was absent but which contained all other essential factors, and as a result they did not grow normally. Pantothenic acid was added to the diet of the control birds. The chickens were infected when 11 to 19 days old by sporozoites or parasitized blood. It was found that blood-induced infections were much less severe in the case of the pantothenic-deficient birds than in the controls. In the former the number of merozoites per segmenter was reduced, a result believed to be due to deficiency of the vitamin and not to defence mechanisms of the host. Stages of the parasite which were affected by the synthetic analogues tested were also affected by pantothenate deficiency in the host and the activity of the former was antagonized by the latter substance. Sporozoite-induced infections in deficient and control groups of birds ran a normal course. In testing synthetic substances against standardized infections produced by sporozoites or parasitized blood it was arranged that in the latter case the peak of parasitemia should occur 4 or 7 days after inoculation. The drug was given in the diet and the birds were kept alternately in light and dark for three-hour periods. The most effective substance tested was pantoyltauramido-4-chlorobenzene which proved much more active than quinine in both types of blood-induced infection. None of the substances showed activity in sporozoite-induced infections. The above substance and 2-pantoyltauramido-5-bromopyridine apparently interfered specifically with the pantothenate metabolism of the blood form of the parasite and possibly with that of the host. The suppressive action of the synthetic substances was in each case antagonized by administration of pantothenate at the same time. The general conclusion is that pantothenate is necessary for the erythrocytic stages of the parasite. Exoerythrocytic stages may possibly find sufficient of this substance in their particular habitat. It is pointed out that these results are specific for *P. gallinaceum* in the chicken host and that the synthetic compounds tested may not necessarily prove active in other types of malarial infection. *J. D. Fulton.*

MARSHALL, E. K., Jr. & DEARBORN, E. H. **A Comparison of Drug-Diet Therapy with Single Daily Oral Dosage in Avian Malaria.** *J. Pharm. & Exper. Therap.* 1946, Oct., v. 88, No. 2, 187–9.

The results obtained by giving sulphonamides for the treatment of infections in such a way that a constant level of the drug is maintained in the blood have established the value of the method in practice. Correspondingly favourable results have been obtained by treating ducks infected with *P. lophurae* in the same way by drug-diet therapy. A comparison has now been made of the results obtained with the above method and that of giving a single daily dose of drug over the same period in this infection. The experimental methods employed by the authors have been reviewed [this *Bulletin*, 1943, v. 40, 223; 1946, v. 43, 826]. The daily oral dose was given in 10 cc. solution or suspension per kilogram for six days, starting, as in the case of drug-diet therapy, 18 hours before infection. The results obtained by both methods are recorded for 19 drugs, including quinine, the minimal effective dose of each drug as well as its quinine equivalent being given. The latter is defined as " the ratio of the dose of quinine to that of the drug under test which produces the same effect on parasitemia." From these experiments it emerged that the best results are not obtained by drug-diet therapy with all drugs, but that, depending on the compound used, the results from a single daily dose may equal, exceed, or prove inferior to those of drug-diet therapy. *J. D. Fulton.*

MARSHALL, E. K., Jr. & DEARBORN, E. H. **The Relation of the Plasma Concentration of Quinacrine to its Antimalarial Activity.** *J. Pharm. & Exper. Therap.* 1946, Oct., v. 88, No. 2, 142–53, 1 fig. [12 refs.]

According to the authors, satisfactory proof has not yet been given that the antimalarial activity of quinacrine (atebrin, mepacrine) is related to the variations in plasma concentrations in persons receiving the same daily dosage. They have studied the action of this drug in ducks infected with *P. lophurae* and obtained evidence that similar plasma concentrations produced in individual birds by different doses are not equally active against the infection and that the differences in plasma concentrations produced by the same dosage are not correlated with antimalarial activity. White Pekin ducks of weight 200 to 3,000 gm. were used and infected according to the technique described by the authors [this *Bulletin*, 1943, v. 40, 223; 1946, v. 43, 826]. The drug was generally given by stomach tube in a volume of 10 cc. per kilogram body weight except in one experiment where the drug-diet method was used. Duplicate analyses for quinacrine were made on blood samples obtained from the right jugular vein and tissues were homogenized in dilute HCl before analysis by the method of BRODIE & UDENFRIEND [this *Bulletin*, 1944, v. 41, 453]. Great variations were found in plasma concentration in individual birds receiving the same dose of drug; and from experimental evidence with single or repeated doses of 75 or 5 mgm. per kilogram, were believed to be due to differences in distribution between plasma and tissues, including erythrocytes. The variation in concentration was less in the case of tissues and was not related to that in plasma. Quinacrine was found to be localized in cells parasitized with *P. lophurae*; in this case also the amounts present were not correlated with levels in plasma and therapeutic effect appeared rather to vary directly with dosage. The rate of disappearance of the drug from plasma and tissues was determined 14 and 28 days respectively after a single dose of 75 mgm. per kilogram and was found to be greatest from plasma and least from liver. The authors believe that their findings in the duck are also applicable to man. *J. D. Fulton.*

TRYPANOSOMIASIS.

VEATCH, E. P., BEQUAERT, J. C. & WEINMAN, D. **Human Trypanosomiasis and Tsetse-Flies in Liberia.** *Suppl. to Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 105 pp.

Part I. *Human trypanosomiasis in Liberia 1941–1944.*

By EVERETT P. VEATCH, M.D.

The first authentic record of trypanosomiasis in Liberia was by THEILER in 1926, who found five cases, following which sporadic cases were noted. The disease is said to have been introduced into Liberia by labourers returning from Fernando Po after the war of 1914–18, but since there is a word for sleeping sickness in most native languages it was probably endemic at a low incidence until the growth of the rubber industry broke down tribal barriers. The development of roads and the stopping of inter-tribal warfare facilitated an alarming increase.

Population distribution in Liberia is greatest along the coast and the French border; between these two areas are stretches where few people live, much of it virgin forest.

In 1941–43 the author investigated the incidence of sleeping sickness in the Western Province of Liberia by a mass campaign. During this period 90,980 persons were examined and 13,481 cases diagnosed. Of these, 67 per cent. received more than six treatments and 33 per cent. less than six. The tribe mainly affected was the Kissi who move freely to visit their fellow-tribesmen in affected areas of Sierra Leone and French Guinea, the tribe being divided almost equally in the three territories. Thirty-one towns located in all parts of the Western Provinces were surveyed.

In 1943, the American Foundation for Tropical Medicine sent Drs. Bequaert and Veatch to do a four-months' survey in North-West Liberia. During this period Dr. Veatch examined 32,617 persons, and found infected a total of 718 cases, or 2·2 per cent. of the population examined. Much of the area covered by this survey had previously been dealt with in the survey and treatment campaign of 1941–43. Details are given of the route covered and the incidence of the disease in the various tribes investigated. (The itinerary is very difficult to follow owing to the absence of a map of Liberia.)

The Kissi showed an incidence of 2·5 per cent. among 1,479 examined. This tribe was examined thoroughly twice during 1941 and 1942, and 26 per cent. had been shown infected. In this new survey, 4 per cent. of the previous Kissi cases were found to have relapsed. The high incidence of infection in this tribe is believed to be due to their cultivation of swamp rice; their migratory habits in visiting their fellow-tribesmen in Sierra Leone and French Guinea; the fact that their towns are small and closely surrounded by vegetation, and possibly the fact that they keep hogs.

It is concluded that trypanosomiasis was present over a wide area in the Western Province, was patchy in distribution and constituted a problem of public health importance.

Analysis of the sex distribution of the disease showed that more men contracted the disease, probably because the nature of their work brought them into close contact with fly. Of the 796 cases diagnosed 14 per cent. were relapse cases, possibly because of insufficient treatment. The disease was most common in the age-group 20–40, probably the result of more frequent exposure to infection. Only 6 per cent. of the cases showed clinically involvement of the central nervous system, 1 per cent. being in the terminal stage, so that a vast majority were in an early stage of the infection. A careful analysis is recorded of the incidence of symptoms and signs, duration of illness from onset, of alteration in cerebrospinal fluid proteins (58 per cent. normal) and cells.

Among the cases diagnosed, 83·94 per cent. received six or more treatments : 10·1 per cent. 1 to 5 treatments ; and 6·03 per cent. did not report for any treatment, probably owing to distance from a treatment centre. Four types of treatment for adults were used, the interval between injections being 5–7 days : (1) Tryparsamide alone, one injection of 1·0 gm. followed by 9 of 2 gm. (2) Antrypol 1 gm., then one injection of tryparsamide 1 gm., followed by tryparsamide 2 gm. for 8 injections. Fainting and vomiting occurred as a result of the antrypol injections in a small number of cases. (3) Antrypol 1 gm. for 3 injections, then tryparsamide 1 gm., followed by 4 doses of 2 gm. Among 686 cases treated with this course arsenical dermatitis occurred in 1·3 per cent., following the first or second dose of tryparsamide, as compared with 0·02 per cent. in a series of 1,928 treated with tryparsamide alone ; albuminuria and oedema of the feet also occurred in this series. (4) Antrypol 1 gm., then tryparsamide 1 gm., tryparsamide 2 gm., then antrypol 1 gm., followed by six doses of tryparsamide 2 gm. With this course no severe dermatitis, nephritis or oedema of the feet was observed. The results of this course of treatment are not yet assessed.

Results of previous treatment were analysed, 35 per cent. of those treated in 1941–42 being examined. 94·35 per cent. were well and had no visual disturbance. In 3·19 per cent. trypanosomes were demonstrated, representing relapses or fresh infections. Death was reported in 1·6 per cent. of the previously treated cases. There was one case of total blindness (0·03 per cent.) and 22 cases (0·79 per cent.) showing dimness of vision. This was found to have come on either after the very early tryparsamide injections when it is liable to be sudden and severe, or after the sixth to tenth injections when the onset is a gradual contraction of the field of vision.

Part II.—*Tsetse-flies in Liberia* : *distribution and ecology* ; *possibility of control.*

By Joseph C. Bequaert.

Dr. Bequaert bases his account of the distribution and ecology of tsetse in Liberia on his observations during 1926 with the Harvard Expedition and during eight months in 1943–44. He commences with a description of the environment in Liberia. The climate is typically tropical throughout with a uniformly high temperature, rainfall and humidity. At the coast the rainfall averaged 138 inches, 80 per cent. falling during May to October, but intermittently also during the dry season. Moving inland, the total annual rainfall diminishes and the dry season is more marked. The relative humidity is high at all times, reaching 98 to 100 per cent. at night in all months near the coast.

Vegetation in the Western Provinces is secondary forest with thick undergrowth and incomplete canopy. In the north-western corner, savannah occurs with fringing forests along the rivers, and streams. Elsewhere swampy forests are common. The mammalian fauna includes many species, mostly small so that fly are generally scarce and man is the chief host. The towns and villages are generally sited on hill tops, surrounded by a large clear area, and therefore free of fly.

Only four species of fly were encountered, viz. :—*Glossina palpalis*, *G. pallicera*, *G. fusca* and *G. nigrofusca*. *G. medicorum* is mentioned as having been caught by McCloy in 1908, two specimens in one area only. *G. palpalis* (*palpalis* form only) occurs throughout the whole of the Western Province and may be found in small numbers on all fair-sized rivers. *G. pallicera* is a tsetse of rain forest and hence is rare or absent from the savannah of Sierra Leone and French Guinea though widespread and moderately common throughout the hinterland of Liberia. It is usually found far from water and attacks man

readily. *G. fusca* is apparently a common fly of the hinterland but becomes rare in the transitional forest and savannah of the north-western corner. It was noted as travelling and feeding in the open ; it attacked man readily and boldly and did not appear to be nocturnal or crepuscular in habit. *G. nigrofusca* was rarely observed, only one being captured, on Harbel Plantation, but specimens were bred from puparia collected in other localities.

Tsetse breeding in Liberia appears to be markedly influenced by the seasons. During the driest months, many pupae were found without much trouble, but from July to October, the months of heavy rain, the ground is water-logged and no pupae, or very few, are to be found. At this time, adult flies are at their peak and climatic conditions favour their dispersion from the rivers even into the villages. Puparia of *G. palpalis*, *G. pallicera* and *G. nigrofusca* were found together apparently under identical conditions. *G. palpalis* pupae were found exclusively in classical breeding places which were small in extent and widely scattered. The breeding requirements of *G. pallicera* and *G. nigrofusca* appear to be the same as for *G. palpalis* since puparia of these species were taken in large numbers together. *G. fusca* pupae were taken only once in deep forest under a fallen tree.

There is a discussion of the possibility of fly control measures. *G. palpalis* is regarded as the sole vector species, and clearings are recommended at river crossings, all wood cover, with the exception of large trees, being removed to a depth of a quarter of a mile from the river on each side and for half a mile above and below the crossing. In the north-western savannah area, eradication of the fly might be achieved by progressive removal of the fringing forest along the river.

Part III. *The treatment of African sleeping sickness with two new trivalent arsenical preparations (Melarsen Oxide and 70A).*

By David Weinman, M.D.

This study was carried out in the Firestone Plantations' Hospital where transmission is not considered to occur, and on patients from different parts of Liberia. These were in poor physical condition, and suffering from malnutrition and other diseases as well as trypanosomiasis.

Melarsen oxide (a trivalent arsenical compound) was well tolerated and produced no toxic reactions. It was active in both early and later stage cases. The dosage employed (0·1 mgm/kgm. orally or intravenously) seemed adequate for early cases, nine being all negative at the end of treatment and not relapsing during periods of observation covering up to six months. Nine neurological cases on the same dosage showed amelioration in all, apparent cures in two, relapse in two, and improvement in five whose cerebrospinal fluid remained abnormal. Oral treatment appeared satisfactory but less effective than parenteral.

The second drug tested, 70A or P. arsenophenyl-butyric acid, is another trivalent arsenical. The dosage employed was 40 mgm. intravenously thrice weekly to a total of 300 to 400 mgm. Ten patients were studied of whom the early cases were negative following treatment for periods up to eleven months. In three cerebral cases the drug was ineffective and did not ameliorate the condition. *T. H. Davey.*

Lapeyssonnie, J. & Lapeyssonnie, L. Trypanosome dans le liquide d'ascite, [**Trypanosomes in the Ascitic Fluid.**] *Bull. Soc. Path. Exot.* 1946, v. 39. Nos. 7/8, 273–6.

This is an account of a case of trypanosomiasis, with the diagnosis of " ascites in an arsenical-resistant case of trypanosomiasis."

Originally in January 1943, the patient, an African woman, had trypanosomes in the blood and gland juice. After treatment with "Orsanine" and Atoxyl, she was seen again in December 1944, now in the second stage, and received further treatment, with Atoxyl and Tryparsamide: by October 1945, despite treatment, she continued to show central nervous manifestations, but although repeated blood examinations were negative, the trypanosomes were found in the gland juice. Clinically, apart from evidence of sleeping-sickness, she had a moderate ascites. Two or three trypanosomes per field were found in fresh and stained preparations of the ascitic fluid. The stools contained many ankylostome eggs.

The author discusses the possible causes and mechanism of the appearance of the trypanosomes in the ascitic fluid, and considers that this is related to the trypanosomiasis, and especially to the persistence of the parasite in the lymphatic system: that it is "veritably a trypanosome seritis", rather than a passive mechanical accumulation. The patient was already in a bad condition, and despite treatment for the relief of the ascites and other complications, she died in October 1945.

The author saw a similar case in 1943, but possesses insufficient details to warrant a report. He believes that the phenomenon is rare and is aware of only one other case in the literature [CHOUMARA, *Revue des Sciences Médicales Pharmaceutiques et Vétérinaires de l'Afrique Française Libre*, Brazzaville]. Full clinical details of the patient's condition and treatment are given, but the point of main interest is the persistence of trypanosomes in the lymphatic system and especially in the ascitic fluid, after they had disappeared from the blood.

[Some years ago, the present reviewer found trypanosomes in enormous numbers in the ascitic fluid of an African patient in Dar es Salaam. The ascites was present when the patient was first admitted, and before diagnosis or treatment had been established; trypanosomes were present in small numbers in the blood on the first direct examination and were only detected in the ascitic fluid afterwards. The trypanosomes could be found without centrifugation, and survived, with active movement, in the fluid, *in vitro*, at laboratory temperature for more than four days. One *M. bancrofti* was found in a fresh preparation of the fluid, and it was suggested that in this case, the transference of the trypanosomes to the ascitic fluid was a secondary phenomenon.]

H. J. O'D. Burke-Gaffney.

MUNIZ, J. & DE FREITAS, G. Estudo sôbre o determinismo da transformação das formas sanguícolas do "Schizotrypanum cruzi" em critídias. 1. Da existência de um fator responsável por essa metamorfose. [**Attempts to discover the Factor necessary for transforming Blood Forms of *T. cruzi* into Crithidia.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Dec., v. 2, No. 12, 995–9. English summary.

The authors made the interesting observation that if *Trypanosoma cruzi* is washed free of all blood constituents before being inoculated to the liquid in fresh N.N.N. medium, the transformation into crithidia forms which usually occurs does not take place. It became evident that some constituent of the blood is necessary for the transformation. Experiments showed that this constituent is in the red blood corpuscles, which are effective when completely washed free of other blood constituents. As the solid part of N.N.N. medium contains blood it is concluded that the holding back of certain constituents in the agar prevents the factor gaining access to the liquid in which growth of the trypanosomes occurs. By removing the liquid part of fresh N.N.N. medium to other tubes and adding various substances before inoculation with washed trypanosomes attempts were made to discover more of the nature of

the missing factor. Nutrient broth, meat infusion and peptone were effective. A blood extract prepared by heating equal parts of blood and physiological saline for 20 minutes at 120° C. was also active when employed alone or when added to the liquid from N.N.N. medium. The extract gave a strongly positive peroxidase reaction. It would appear that the X factor is necessary, but only in part, as the liquid of N.N.N. medium contains abundant haemoglobin. Meat infusion, nutrient broth and peptone will not alone determine the transformation, owing to lack of X factor. Further investigations are being carried out to determine the nature of the active substance. *C. M. Wenyon.*

Seijas Rivas, J. V. Contribución al estudio de la enfermedad de Chagas, en el Estado Carabobo. [**Chagas's Disease in the State of Carabobo.**] *Bol. de los Hospitales.* Caracas. 1946, Mar.–June, v. 45, Nos. 2/3, 61–93, 13 figs. [35 refs.]

This account of field investigations into Chagas's disease, carried out during a period of 3½ years, was presented by the author as his thesis for the Doctorate of Medicine. The inhabitants of the area studied lived in small hamlets, in rush and palm-thatched huts, dilapidated in many cases, sharing their quarters with domestic animals, living, in short, in squalor and poverty. Their food comprised mainly kidney beans, plantains, yams and the like.

The chief vectors of *T. cruzi* were *Rhodnius prolixus*, of which a large proportion, half or even more, were found infected in different districts; *Panstrongylus geniculatus*, also infected, and *Psammolestes arthuri* were present, but none of the last was found infected. Opossums and armadillos were proved to be reservoir hosts.

Diagnosis of cases was made by the clinical condition and confirmed by direct examination of the blood (thick drop) and by xenodiagnostic methods. Nine cases are described in detail (10 are referred to), all in children whose ages ranged from 2½ months to 16 years. They were all typical. [No figures are given by which one can calculate the actual prevalence of the disease. The illustrations are very foggy and poorly reproduced.]

H. Harold Scott.

LEISHMANIASIS.

Feldman, A. **Kala-Azar with Onset of Symptoms in Great Britain.** *Brit. Med. J.* 1946, Nov. 30, 816–17.

The object of this paper in which is described a typical case of kala azar is to call attention to the recognition of this disease in English soldiers returning from the Mediterranean littoral. In this case the patient was a soldier who had served in North Africa and Italy for 3½ years, returned to England in good health and remained so for four months. The incubation period should be noted and it was probably considerably longer than suggested. The diagnosis was made by sternal puncture and treatment successfully conducted by 21 intramuscular injections of anthiomaline. *P. Manson-Bahr.*

Parrinello, G. Contributo allo studio della diatesi emorragica nella Leishmaniosi infantile. [**The Haemorrhagic Condition in Infantile Kala Azar.**] *Pediatria.* 1946, July–Sept., v. 54, Nos. 7/9, 432–44. [21 refs.] English summary (9 lines).

It is well known that certain cases of kala azar are specially liable to haemorrhages. From this point of view the author has examined 21 cases of

the infantile disease with particular reference to the condition of the blood and bone marrow. The results of these investigations are set out in two comprehensive tables, while short histories of the 21 cases are given. All cases showed a reduction in the number of blood platelets, an increase in the haemorrhagic time, a slight increase in the coagulation time and delay in contraction of the blood clot. In 12 of the cases the blood pressure was low. The author supposes that a number of factors are responsible for these conditions, such as alterations in the structure of the blood vessels, changes in the spleen and bone marrow and modifications in the body metabolism.

C. M. Wenyon.

MAKARI, J. G. **Cephalin-Cholesterol Flocculation Test in Kala-Azar.** *J. Trop. Med. & Hyg.* 1946, Dec., v. 49, No. 6, 113–14, 1 fig.

"(1) The cephalin-cholesterol flocculation test was done on sera of eight patients with infantile kala-azar. A strong positive reaction was obtained in the eight cases studied, five had a ++++ reaction, two +++ and one a ++ reaction.

"(2) The three cases followed after treatment remained positive with Hanger's test, whereas the serial dilution method showed a fall in the titre.

"(3) Strong positive reactions in kala-azar lend support to my contention that the CCF test is an index of selective reticulo-endothelial activity."

CHOUDHURI, R. K. S. **Observations on the Treatment of 25 Cases of Kala-Azar with Stibatin (Sodium Antimony Gluconate).** *Indian Med. Gaz.* 1946, Apr.–May, v. 81, Nos. 4/5, 174–6.

The 25 cases referred to in the title varied in age from 10 to 50 years. Treatment consisted in intramuscular injections in 16 and intravenous injection in 9 cases. The injections were given on alternate days, the dosage for an adult of 8 stone being 10 cc. for each injection till a maximum of 200 cc. had been given. In all cases the drug was tolerated without toxic symptoms. The cure rate for 23 cases (one of the 25 died of cerebral malaria and one could not be followed) was 22, or 95·65 per cent. The one case which was not cured was treated with urea stibamine.

C. M. Wenyon.

FORT & ZOTTNER. Un cas de kala-azar traité par un composé non stibié. [**Case of Kala Azar treated with a Non-antimonial Compound.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 170–73.

The case reported is that of a man who became ill 2 years after his arrival in Morocco. He was running a fairly continuous fever for eighteen months, associated with enlargement of the liver and spleen, which remained undiagnosed in spite of seven long stays in hospital. Finally kala azar was suspected but bone marrow puncture failed to reveal leishmania. Treatment with a diamidine (M.B.800) was instituted. Response was almost immediate. The course was repeated two months later, after which the patient's good health was maintained. It would appear that a diagnosis of kala azar was justified.

C. M. Wenyon.

GELLHORN, A. & VAN DYKE, H. B. **The Correlation between Distribution of Antimony in Tissues and Chemotherapeutic Effect in Experimental Leishmaniasis.** *J. Pharm. & Exper. Therap.* 1946, Oct., v. 88, No. 2, 162–71, 3 figs. [12 refs.]

A survey of the literature on the chemotherapy of leishmaniasis with antimonials shows that pentavalent compounds are, for reasons not known, more

effective and less toxic than tervalent types. The investigations now described sought to find if any correlation exists between the therapeutic activity of a drug and the amount of antimony present in tissues normally parasitized by leishmania. For practical reasons antimony estimations were limited to that present in liver and spleen. Eight tervalent and seven pentavalent antimonials were used in these studies. The excretion and tissue-distribution of some of these compounds as well as the method of estimating antimony have recently been described by the authors [this *Bulletin*, 1947, v. 44, May]. The methods of chemotherapeutic testing employed are those in general use. In the case of tervalent compounds, there was a greater localization in liver relative to dosage than occurred with the pentavalent compounds. In the spleen the results were reversed ; in this case the degree of localization was possibly accounted for by the amount of antimony administered. Only three pentavalent compounds, Stibanose, Neostibosan and Neostam, were effective in freeing the liver and spleen from parasites as judged from imprints of these organs [no culture methods appear to have been employed in detecting the presence of parasites]. It was not established that the tervalent compounds significantly reduced the degree of infection. There was some correlation between the tissue-concentration of antimony and the degree of parasitization in so far as the parasite numbers approximated to those in control animals when the amount of antimony present was negligible. The presence of a high concentration of the metal was, however, not synonymous with activity and this was specially true of Stibacetin with regard to the spleen. Nevertheless for an antimonial to be effective a high concentration in spleen is deemed necessary. There is a short discussion on the relation of chemical structure to activity in the case of pentavalent antimonials. • *J. D. Fulton.*

Timpano, P. Sulla trasmissione della leishmania tropica all'uomo. (Ricerche sperimentali.) [**Transmission of Oriental Sore to Man.**] *Policlinico.* Sez. Prat. 1946, Sept. 30–Oct. 7, v. 53, Nos. 39/40, 813–19, 6 figs. [20 refs.]

The author describes experiments he carried out in Calabria during the four years 1940–1943, on the transmission of oriental sore by house flies, mosquitoes and sandflies. His procedure was to keep the insects in a small cubical cage, the bottom of which was covered to allow only an area of 1 sq. centimeter through which the insects could feed. In each experiment two insects were used. The cage was first fixed over an oriental sore for two nights and then transferred, presumably without interval, to the arm of another person and left there for a similar period. In this way, attempts at transmission were made 32 times with house flies, 29 times with mosquitoes and 31 with sandflies. It is claimed that in three of the experiments with mosquitoes and in one of those with sandflies, oriental sore was transmitted. It is further claimed that examination of the insects after the experiment revealed leishmania in the pharynx and stomach of two mosquitoes and the sandfly. The incubation period in the four successful experiments varied from 12 to 15 days. In 30 to 40 days the initial lesions became typical oriental sores. Four photographs show oriental sores on the arms of those experimented upon, while three microphotographs purport to show leishmania in the insects. The failure to transmit infection by the houseflies is explained by the fact that the oriental sores on which the insects fed were in the ulcerating stage, which necessitated deep probing such as that carried out by mosquitoes and sandflies, for parasites to be taken up. The author concludes that his experiments do not exclude the possibility that house flies may, under certain circumstances, transmit the infection. [The arrangements of the experiments would seem to be calculated to favour mechanical transmission rather than transmission depending on development of flagellates

in the flies. Furthermore the insects were evidently wild ones, but infection of four with *Leishmania tropica* before the experiments is hardly probable in view of the rarity of cases of oriental sore in the district. It is perhaps remarkable that the incubation period should have been as short as two weeks in all four cases. It is not possible from the microphotographs to recognize leishmania in the infected insects which the author does not definitely identify with those which are supposed to have transmitted the infection.]

C. M. Wenyon.

Pessôa ,S. B. & Barretto, M. P. Tipos de exploração do solo como fator de incidência da leishmaniose tegumentar Americana. [**The Soil as a Factor in the Causation of American Cutaneous Leishmaniasis.**] *Brasil-Medico.* 1946, Sept. 21 & 28, v. 60, Nos. 38/39, 305–9. [19 refs.]

This contribution is a general summary of the evidence that workers employed in forestry and wood industries, as in making railway sleepers, chicleros (gatherers of chicle gum), etc., are those most prone to infection. The synonyms of this disease—forest yaws, bosch-yaws, pian bois—are evidence of the connexion recognized to exist. The men build log huts where they work and these allow swarms of Phlebotomus to enter. The authors quote abundantly from the literature in support of their statements. *H. Harold Scott.*

Romaña, C., Conejos, M. & Lizondo, J. E. Foco de leishmaniosis tegumentaria en Tucumán. [**A Focus of Cutaneous Leishmaniasis in Tucumán.**] *An. Inst. Med. Regional.* Tucuman, Argentine. 1946, Aug., v. 1, No. 3, 239–87, 25 figs. & 1 map. [Summary in English by the author.]

" The authors report the finding of a focus of cutaneous leishmaniasis in the Department of Burruyacú (Tucumán). Twenty-one cases are reported, the majority of them children from 7 to 14 years old. From a clinical point of view, the lesions were similar: an ulcerous form with a great tendency to a spontaneous cure. Generally the mucous membranes of the mouth and nose remain healthy.

" The histologic study of the biopsies revealed the well known leishmaniasis histo-pathology, the authors stressing the frequent finding of " mastzellen " in the interior of the cellular infiltration.

" The patients were treated with *Fuadine, Urea-Stibamine, tartar emetic* and *Repodral.* In the area, *Ph. migonei* and *cortelezzi* have been identified."

FEVERS OF THE TYPHUS GROUP.

On some Anomalous Weil-Felix Reactions.

Note by Sir John W. D. Megaw, *Sectional Editor.*

Some readers of this *Bulletin* have doubtless been puzzled by anomalous responses to the Weil-Felix test which have been reported from time to time.

Dr. A. Felix, in a personal communication, has made important comments on some of these and has now kindly agreed to the publication of the substance of his remarks. Special reference was made to two papers, one by van Rooyen [see this *Bulletin*, 1945, v. 42, 194] in which a number of cases are discussed in which the reaction was of the *Proteus OX2* type, although there was no suspicion of tick-borne typhus; the other was by Dick [see this *Bulletin*, 1946, v. 43, 726] who reported several different kinds of anomalous reaction

including :—" relatively common " non-specific *OXK* reactions at titres of 1–480 or over; cases of murine typhus in which the *OX2* titres were higher than the *OX19* ; and rising titre reactions of the *OX19* and *OX2* type in fevers of the enteric group and other fevers.

Dr. Felix states that workers having inside information know that the " Standard R.A.M.C. Suspensions of the *Proteus OX* Strains " during 1941–1943 in the Middle East have not been of very good quality owing to their having had to travel across or round Africa, and that many batches were therefore useless on arrival. He also states that the *OXK* suspensions were the first to deteriorate, next came *OX2*, while *OX19* was relatively stable.

These comments, from so authoritative a source, deserve the widest publicity ; they also raise the question of the great need for standardization of the materials and methods employed in the Weil-Felix test, which is often the only available means of diagnosis of the fevers of the typhus group.

Proteus cultures, dried *in vacuo* and stored in the powdered form in ampoules, are said to keep indefinitely ; such dried preparations can therefore be used with confidence for making suspensions.

The matter is of such importance that it deserves study by an international committee constituted on the lines of the Biological Standardization Committee of the Health Organization of the League of Nations.

Bol. Oficina Sanitaria Panamericana. 1946, May, v. 25, No. 5, 385–7. [English summary 393.] Primera Reunión Interamericana del Tifo. [**First Inter-American Meeting on Typhus.**]

" The First Inter-American Meeting on Typhus was held in Mexico, October 7–13, 1945, under the auspices of the Mexican Government and with the co-operation of the Pan American Sanitary Bureau and the Institute of Inter-American Affairs. Delegates from Colombia, Cuba, Chile, Guatemala, Mexico and the United States attended. Recommendations were made on better reporting of the disease and the initiation of better control measures based on the use of vaccines and DDT. It was also recommended that surveys be intensified in order to increase our knowledge of the clinical types of rickettsiasis present in the different regions of the Americas. Prevention, diagnosis, treatment, and epidemiological aspects of the disease, especially means of transmission and maintenance of the virus in nature, were given special attention and recommendations made."

Montoya, J. A. Datos sobre la distribución e incidencia de las rickettsiasis en las Américas (Comisión Panamericana del Tifo). Septiembre de 1945. [**Data on Distribution and Incidence of Rickettsiasis in the Americas.**] *Bol. Oficina Sanitaria Panamericana.* 1946, May, v. 25, No. 5, 394–9, 1 map. [English summary, 402.]

Tovarnickij, V. I., Krontovskaja, M. K. & Ceburkina, N. V. **Chemical Composition of** *Rickettsia prowazeki.* [Correspondence.] *Nature.* 1946, Dec. 21, 912.

Potop, I. & Bals, M. La polypeptidémie dans le typhus exanthématique. [**Polypeptide Levels in Exanthematic Typhus.**] *Bull. Acad. Med. Roumanie.* 1945, v. 17, Nos. 1/3, 216–20.

The following is a translation of the authors' summary.

It is noted in general that in exanthematic typhus, polypeptides and urea are increased and the alkaline reserve and chlorine are diminished.

The toxic syndrome of exanthematic typhus is not due to a single factor and we have observed that no constant single factor exists in relation to the gravity of the condition. It should, however, be noted that in every case and

especially in serious fatal cases, there are important variations, sometimes due to one factor, sometimes to another, and sometimes to all the factors together, which undoubtedly contribute between them to the lack of equilibrium in the humoral fluids. *H. J. O'D. Burke-Gaffney.*

BENGTSON, Ida A. **Serological Relationships in the Epidemic-Endemic Typhus Group as determined by Complement Fixation.** *Pub. Health Rep.* Wash. 1946, Sept. 20, v. 61, No. 38, 1379–85.

The author describes a further, and more extensive, investigation into the complement-fixing properties of sera of guineapigs convalescent from attacks of epidemic and endemic typhus fever.

Three strains of endemic and sixteen of epidemic rickettsiae were studied; the former were the Wilmington strain, isolated from a patient by MAXCY in 1928 and two strains isolated from rats in the U.S.A.; the latter originated from Prague (the Breinl strain), Madrid, Barcelona, Colombia, Egypt, Teheran, and Algiers.

The antigens were prepared from yolk-sac cultures by a modification of Craigie's ether method; the immune sera were obtained from guineapigs two to three weeks after recovery from febrile attacks occurring in the course of the maintenance of the various strains.

All the epidemic antigens were titrated against a Breinl strain of immune serum; for the titration of the endemic antigens the Wilmington strain of serum was used.

Various strains of epidemic and endemic immune sera were tested against fixed amounts of antigen of different strains. From the detailed results shown in tabular form it appears that there was a remarkable degree of uniformity in the complement-fixation titres of the different strains of epidemic immune sera, and a similar uniformity among the titres of the endemic sera. For example, the Breinl and two other epidemic sera all gave titres of 1–128 when tested against seven different strains of epidemic antigens, and the same sera tested against endemic antigen strains gave titres of 1–32 against two, and nearly 1–64 against the third.

Two endemic sera were tested in the same way against endemic and epidemic antigens; with the endemic antigens the titres ranged from 1–128 to 1–256; with epidemic antigens the range was 1–32 to 1–128, but in each individual test the titre with the homologous antigen was two to three times higher than with the heterologous.

The conclusion reached was that although epidemic and endemic typhus fevers possess an antigenic factor common to both the diseases can be differentiated by the uniform occurrence of a higher-titre complement-fixation reaction against the homologous antigen than against the heterologous.

[This conclusion is doubtless justified when the tests are carried out by workers with exceptionally high standards of technical skill, experience, and laboratory facilities, such as were at the service of the author; but the potential margin of error seems too small to compensate for any shortcomings in these respects.] *John W. D. Megaw.*

CODELEONCINI, E. Studi e ricerche su uno speciale virus tifico d'origine umana isolato in Etiopia. [**Investigation of a Special Type of Typhus Rickettsia of Human Origin, isolated in Ethiopia.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, v. 6, Nos. 1/2, 107–27. [24 refs.] English summary (4 lines.).

A strain of typhus rickettsia isolated in Addis Ababa is claimed to be the first in Ethiopia that has been clearly proved to be murine.

The strain was consistently orchitic; it was maintained through 72 consecutive passages in guineapigs.

Among 200 clean lice fed on the patient on the 5th day of his illness 4 per cent. became infected. By intrarectal inoculation from louse to louse, the infection rate rose to 100 per cent. and the fatality rate for lice, which at first was 20 per cent., rose to 55 per cent.

Numerous animal inoculations were carried out. In successive passages the strain became progressively more virulent for guineapigs and lice, but less virulent for rats, so that there was a tendency to the development of the characteristics of the classical type of infection. *John W. D. Megaw.*

Davis, D. E. & Pollard, M. **The Distribution of Murine Typhus in Rats and in Humans in San Antonio.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 619–24, 1 fig.

In a survey of murine typhus among rats and human beings it was found that there was a general, but not detailed, correlation between the number of cases in human beings and the percentage of rats found infected by complement fixation tests. Human infection seemed to depend on local concentrations of infected rats rather than on uniform distribution of infection among the rats of the whole area.

In " fairly good residential areas " about 40 per cent. of the rats were infected; in slum areas the infection rate was 60 per cent. *John W. D. Megaw.*

Pollard, M., Davis, D. E. & Olson, T. A. **The Serological Detection of Murine Typhus in Flea Feces.** *Amer. J. Hyg.* 1946, Sept., v. 44, No. 2, 244–8, 1 fig.

The authors describe a new test for detecting murine-typhus infection in rat fleas. They find that suspensions of infected flea faeces contain a specific antigen whose presence can be shown by the occurrence of positive complement-fixation reactions when the suspensions are tested against a homologous immune serum. The specificity of the test is shown by the fact that negative reactions always occurred when suspensions known to contain the antigen were tested against immune sera of tick typhus, mite typhus, and Q fever.

The test is claimed to be more rapid and less costly than the inoculation of animals with flea suspensions, and also to be more reliable than the commonly-used complement-fixation test of rat serum, because this shows only the presence of immune bodies, which persist after the animal has ceased to be infective.

Details of the technique will be found in the paper. The procedure in outline consists in placing 10 or more undamaged fleas from one or two freshly-killed rats in a test tube, which is kept overnight in the vertical position at room temperature. The suspension is made by mixing 0·6 cc. of normal saline with the faecal deposit in the tube.

Positive results were obtained with 13 out of 17 suspensions each of which was made from a pool of fleas collected from an experimentally-infected rat.

Control suspensions, from fleas of 22 non-infected rats, gave 20 negative results; the remaining two were anticomplementary.

Flea-faeces suspensions originating from 30 serum-positive trapped rats yielded 14 positive, 11 negative, and 5 anticomplementary, results.

Suspensions from 53 serum-negative trapped rats gave 51 negative, and 2 positive, results. *John W. D. Megaw.*

Ruiz Sanchez, F., Ponce de Leon, Estela & Orozco, G. La frecuencia del tifo en Guadalajara. [**The Frequency of Typhus in Guadalajara.**] *Medicina.* Mexico. 1946, Oct. 25, v. 26, No. 518, 440–42.

Typhus is common in Guadalajara, Mexico. The predominant variety is a benign, endemic murine form, having widely varying clinical manifestations.

The authors set out to discover the incidence of *Proteus OX19* agglutinins in persons without clinical evidence of the disease.

They carried out Welch's modification of the classical Weil-Felix reaction on 705 specimens of blood from afebrile persons. Amongst these, 114, or 16·2 per cent., were positive. Titres of 1/50 or over were observed in 78 cases.

The authors conclude that rickettsial infection is frequent in Guadalajara, but is not always recognized. *H. J. O'D. Burke-Gaffney.*

Bengtson, Ida A. **Separation of the Complement-Fixing Agent from Suspensions of Yolk Sac of Chick Embryo infected with the Karp Strain of Tsutsugamushi Disease (Scrub Typhus).** *Pub. Health Rep.* Wash. 1946, Sept. 27, v. 61, No. 39, 1403–8.

It has been reported previously that a complement-fixing antigen is present in yolk-sacs infected with the Karp strain of scrub typhus rickettsiae. This paper describes the technical details of a method whereby an almost water-clear fluid containing the greater part of the antigenic fraction can be obtained. The methods used included ether treatment, differential centrifugation, and iso-electric precipitation, of yolk-sac suspensions. *A. J. Rhodes.*

Giroud, P. Pouvoir pathogène des corps homogènes, formes de résistance des agents étiologiques de la fièvre fluviale du Japon ou du typhus des broussailles. [**The Pathogenicity of the Homogeneous Bodies—Resistant Forms of the Causative Agent of Japanese River Fever or Scrub Typhus.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 267–70, 4 figs. on 2 pls.

The author describes observations on the relationship between the morphological appearance and pathogenic properties of two strains of rickettsiae of tsutsugamushi disease. His general interpretation of the findings is on the same lines as in his earlier work on other typhus rickettsiae.

The morphological investigation was carried out chiefly on smears from the peritoneal exudate of infected mice. The smears were fixed, treated with acetone, and stained with Giemsa R.A.L. which was freshly diluted with boiling water squeezed out from a tampon of cotton wool.

The rickettsiae, as usual, were polymorphic; they sometimes occurred in clusters both in the protoplasm and nuclei of the invaded cells.

Strains kept for 15 days at −25°C. showed a loss of virulence: they no longer killed the mice but still caused great enlargement of the spleen and a peritoneal exudate in which there were large mononuclear cells with vacuolated protoplasm and nuclei, but no rickettsiae, could be seen. After further passage through mice, the strain regained its virulence.

Intracutaneous injections of the strain into rabbits caused local reactions which were proportional to the degree of concentration of the rickettsiae; with large doses necrosis was caused.

Strains inoculated intranasally into rabbits caused bronchopneumonia, but rickettsiae were found only in the form of homogeneous bodies of 2–3μ in diameter and of a prussian-blue colour when stained with Giemsa.

Material containing these bodies when inoculated into mice caused an attenuated reaction, but after a second passage through mice typical reactions were obtained.

"The evolution—rickettsia bodies to homogeneous rickettsiae" is thus regarded by the author as being obtainable by the simple method of passage from mouse to rabbit and *vice versa*. *John W. D. Megaw.*

PHILIP, C. B. & WOODWARD, T. E. **Tsutsugamushi Disease (Scrub or Mite-borne Typhus) in the Philippine Islands during American Reoccupation in 1944–45. II. Observations on Trombiculid Mites.** *J. Parasitology.* 1946, Oct., v. 32, No. 5, 502–13, 6 figs. [20 refs.]

The authors present facts on the systematics and biology of Trombicula and related mites in the Philippine Islands. Larvae of *T. akamushi* and *deliensis* both attack man, as does *T. wichmanni*, and possibly one or two others. "Scrub Itch" does not occur in these islands.

It is generally accepted that larvae of *akamushi* and *deliensis* are very similar: the generally accepted criterion in that in the first the dorsal setae are more than 30, and that there are 8 setae in two (or even three) of the rows: in *deliensis* there are generally 28, and they reach 8 in only one row (the second). The authors find both types, and a very large number of others occur. A considerable proportion of specimens are asymmetrical, having 7 or 9 setae in a row in place of an even number. The authors do not analyse their biometrical data very far; probably wisely, for until other instars of *akamushi* and *deliensis* are available it seems unwise to concentrate on chaetotaxy of larvae which cannot be identified with certainty. One notices that both types of larvae occur on a number of sorts of *Rattus*, also on shrews.

The authors did not spend long in the Philippines and regard it as probable that many more Trombiculinae remain to be discovered. They give a key, which includes the larvae known to occur or most likely to be discovered.

P. A. Buxton.

SAYEN, J. J., POND, H. S., FORRESTER, J. S. & WOOD, F. C. **Scrub Typhus in Assam and Burma. A Clinical Study of 616 Cases.** *Medicine.* 1946, May, v. 25. No. 2, 155–214, 27 figs.

In this well-illustrated paper of 60 pages the authors give an exceptionally clear and comprehensive account of the clinical aspects of scrub typhus in Assam and Burma, from November 1943 to February 1945.

The study is based on observation of 616 patients, of whom 81 were Chinese and the rest Americans.

A statistical analysis deals with 200 consecutive American cases seen between April and October 1944. [All the figures enclosed in brackets in this abstract refer to percentage incidence among these 200 cases and it must be noted that they were of greater average severity than those seen before and after the above period.] The fatality rate (8·5) was about twice as high as the average for the whole series. Variation in severity of the disease is shown by the wide range of fatality rates among different groups of patients—0 to 16 per cent.

From the wealth of valuable information contained in the paper only a few items can be mentioned.

During the first week of the illness it was not usually possible to tell whether the attack would be severe or mild: the severe and fatal attacks (33) differed little from the mild and moderate (67) at this stage. Death occurred most frequently in the early part of the third week, and often happened a few hours after the onset of convulsions, pulmonary oedema, or severe cyanosis. At autopsy the usual widespread pathological changes were found, but gross tissue destruction was rarely seen.

The intraocular findings during life included:—engorgement of the retinal veins (67); oedema of the retina and disc (36); and retinal haemorrhage (6·6).

The primary lesion (60) had seldom been noticed by the patient, and often had to be carefully looked for. The rash (71) was usually maculopapular; it involved the trunk in all cases, often also the limbs, but never the palms or soles.

The fever was usually of an irregular spiking type with a double daily rise at some stage of the illness. No relapses occurred.

The spleen was often palpable (35) and sometimes was also tender (7·5).

The haemoglobin fell to some extent during the first two weeks; occasionally by 25 per cent. The leucocyte count was very variable; a moderate increase in the polymorphonuclears and lymphocytes was usual.

An *OXK* titre of 1–100 was regarded as diagnostic because this titre was not observed in any other condition, but it was reached in only about half of the cases. *OX2* and *OX19* titres, up to 1–50 at most, were not infrequent early in the illness.

Among the most useful diagnostic points were:—(*a*) history of exposure to risk; (*b*) the primary lesion; (*c*) increasing lymphadenopathy (97), but this was seen in several other diseases; (*d*) the rash; (*e*) the intraocular signs; (*f*) an *OXK* titre of 1–100 or over; and (*g*) exclusion of cerebral malaria, pneumonia, meningitis, typhoid fever, plague and sepsis.

It was believed that some degree of pulmonary involvement was usually present; pronounced tachypnoea and severe cyanosis indicated severe and dangerous pneumonitis which might not be revealed by X-ray examination.

In severe attacks cardiac enlargement with gallop rhythm was common, but not more so in fatal cases than in severe attacks followed by recovery. The only electrocardiographic finding regarded as indicating myocarditis was a sharp T-wave inversion or notching, which was found in 11 per cent. of 61 acutely ill patients, but, surprisingly, none of the patients who had this condition died, whereas there were three deaths among the other patients whose curves had been found free from the abnormality shortly before death. It appeared, therefore, that no prediction could be made of impending cardiac disaster.

Among the numerous disturbances referable to the nervous system were:—meningeal signs (13·5); transient mental confusion (22); delirium (13); definite delusions (3·5); "malignant restlessness" (13); convulsions (6); incontinence of urine or faeces (7); persistent hiccough (4); and Cheyne-Stokes breathing (7). Some degree of deafness, usually disappearing with defervescence, was usual.

Albuminuria was usual; when pronounced (24) it was commonly associated with the presence of brown-yellow granular casts. A few red blood cells were sometimes found in the urine (9). Oliguria (13) was regarded as occurring when the urine was less than 500 cc. daily, it was sometimes accompanied by oedema, and was present only in severe attacks. Other features of grave and fatal illness were:—ascites (3·5); blood urea nitrogen in excess of 50 mgm. per cent. (7); and severe hypochloraemia—less than 500 mgm. per cent.

Haemorrhages (28) occurred in all the fatal, and in more than half of the grave, cases; the types were:—subconjunctival (9); epistaxis (5); haemoptysis (4); oral (3·5); ecchymosis (2·5); intestinal (2·5), including two of massive type; subarachnoid (0·5); and retroperitoneal (0·5).

The most ominous phenomena were as follows (the first figure in each case shows the number of patients who died afterwards, the second figure refers to the number of patients affected):—convulsions, 11–12; Cheyne-Stokes breathing, 12–14; hiccough 5–8; temperature 105°F. on five days, 13–24; malignant restlessness, 13–26; tachypnoea (36 per minute for seven days) 10–22; tachycardia (over 130 per minute) 12–27; and cyanosis 14–36.

Important complications during the two weeks following defervescence were:—severe intestinal haemorrhage in one case; thrombophlebitis sometimes

occurred, and in three cases it was followed by pulmonary embolism; post-typhus pleurisy occurred in 10 per cent. of the cases; all the patients affected by these complications recovered.

The cardiac condition of 25 unselected patients was studied in late convalescence; no evidence of damage was found in any case, but no patients who had been gravely ill were available for examination.

The treatment was on orthodox lines, including complete rest in the semi-Fowler position; a generous diet, which often had to be fed to the patient; a fluid intake of at least three litres daily; and skilled nursing. No hesitation was felt in giving 5 per cent. glucose by the vein in the rare cases in which it was considered necessary; blood transfusions were also given in accordance with the usual indications. Digitalis or other drugs to combat myocardial damage was never found necessary. Penicillin and convalescent serum were tried but no benefit was observed from either.

An air-conditioned hospital was installed in June 1944; it added greatly to the comfort of the patients and attendants.

After experience had been gained by "trial and error" the last 300 of the surviving American patients were finally disposed of as follows:—82 per cent. were returned to full duty within three to four months; the rest were invalided, mostly because of the severity of the attacks, but a few who had been classed as "mild or moderate" were invalided for reasons other than scrub typhus.

John W. D. Megaw.

STEINITZ, H. **A Case of Tick Borne Fever (Fièvre Boutonneuse) in Palestine.** *Harefuah.* Jerusalem. 1946, Dec. 1, v. 31, No. 11. [In Hebrew 189–90, 1 fig. English summary 190–91.]

This is stated to be the first case of this disease known to be published in Palestine.

CODELEONCINI, E. Sulla presenza in Etiopia della "Rickettsia Weigli" Considerazioni sul rapporto fra la Rickettsia Weigli, l'agente eziologico della "Febbre delle Trincee" e la Rickettsia pediculi. [**The Occurrence in Ethiopia of "*Rickettsia weigli*" the Rickettsia of Trench Fever.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, v. 6, Nos. 1/2, 129–51. English summary (9 lines).

A laboratory outbreak of trench fever occurred at the Addis Ababa Rickettsiosis Laboratory. All the seven persons affected were attacked while they were employed in supplying blood meals for thousands of lice which were being reared for the purpose of preparing the Weigl type of vaccine. The first case occurred on the 25th October, 1941, about eight days after it had been discovered that some lots of "clean" lice were harbouring rickettsiae: the last case appears to have occurred some time in December.

The clinical features in each case were typical of trench fever; 6 or 7 short paroxysms of fever recurred at an average interval of 4·5 days. The nature of the infection was demonstrated by intraperitoneal inoculation of two monkeys with the intestines of 40 lice taken from batches found infected by rickettsiae. The monkeys developed typical recurrent febrile attacks, and a third monkey reacted to inoculation with blood from one of them.

Guineapigs inoculated intraperitoneally with infected lice or sera from patients developed irregular febrile attacks but rickettsiae were not found in peritoneal scrapings.

Rickettsia-agglutination tests were carried out on the patients, with organisms obtained from infected lice; the titres observed ranged from 1–20 to 1–320.

As a result of extensive laboratory investigation of the strain the author concluded that it was identical with *Rickettsia quintana*, otherwise known as

R. weigli, *R. wolhynica* and *R. pediculi* Rocha-Lima. He also regarded the disease as being the same as that described by Mosing in Poland, and Weigl's disease.

[The English translation of the summary is unhappy in its description of the outbreak as one of "typhus". Unfortunately the illustrations referred to in the text have not been reproduced; they would have added greatly to the value of the paper, which is an important contribution to the knowledge of trench fever.] *John W. D. Megaw.*

YELLOW FEVER.

Fernández, E. Situación de Venezuela en relación con la fiebre amarilla. [**The Yellow Fever Position in Venezuela.**] *Bol. Oficina Sanitaria Panamericana.* 1946, June, v. 25, No. 6, 516–18, 1 map. English summary.

Muñoz, N. T La situación de la fiebre amarilla en Bolivia. [**The Yellow Fever Position in Bolivia.**] *Bol. Oficina Sanitaria Panamericana.* 1946, June, v. 25, No. 6, 512–15, 3 maps. English summary.

Bates, M. & Roca-Garcia, M. **An Experiment with Neurotropic Yellow Fever Virus in Saimiri Monkeys and Haemagogus Mosquitoes.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 607–12. [10 refs.]

In a previous paper [in the press] Bates and Roca-Garcia showed that haemagogus mosquitoes rarely become infected from feeding on Saimiri monkeys injected with a pantropic strain of virus which has undergone six mouse-brain passages. This failure might be due either to changes in mosquito adaptation of the virus or to reduced circulation of virus in monkeys inoculated with such a passage strain.

In an attempt to clarify these points, passage of French neurotropic virus of the 250th mouse brain passage was carried out in Saimiri monkeys. The first monkey received 159 mouse m.l.d. of virus and the maximum amount of virus was found to be circulating on the 4th day following intramuscular injection. Blood was removed at this stage and 0·03 cc. of 1 : 10 dilution was injected into a second Saimiri monkey. Twenty-two Saimiri passages were made in this manner when the experiment was discontinued. The dose of virus inoculated varied from 5 to 51,000 mouse m.l.d. but this did not appear to influence the final result. The monkey receiving five mouse m.l.d. died on the 6th day and that receiving 51,000 survived. No alteration in virulence or adaptation for the Saimiri occurred as a result of passage. The virus showed no demonstrable change in behaviour on white mouse inoculation in the course of these passages.

The Saimiri monkeys of the serial passage experiment were used as source animals for eight infection experiments with haemagogus mosquitoes. All attempts to recover virus by inoculation of mosquitoes into mice, by inoculation of pools of mosquitoes into monkeys and by feeding mosquitoes on baby mice or on Saimiri monkeys, were negative with one exception. The authors consider this was probably an accidental infection.

In 1932, Davis *et al.* [see this *Bulletin*, 1933, v. 30, 355] found difficulty in infecting *Aëdes aegypti* on rhesus monkeys circulating virus of a fixed neurotropic strain but they were able to obtain some mosquito transmissions. It is considered that this reflects the much greater susceptibility of *Aëdes aegypti* to virus infections in general. *F. O. MacCallum.*

ANDERSON, C. R. & OSORNO-MESA, E. **The Laboratory Transmission of Yellow Fever Virus by** *Haemagogus splendens*. *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 613–18, 1 fig. [11 refs.]

It is obviously of importance to know whether all different species of Haemagogus mosquitoes found in South America are potential vectors of yellow fever virus. *Haemagogus spegazzinii falco* has been shown to be of epidemiological importance in jungle yellow fever in Colombia [BUGHER *et al.* this *Bulletin*, 1944, v. 41, 475] and recently WADDELL and TAYLOR [this *Bulletin*, 1946, v. 43, 33] have obtained transmission by *Haemagogus equinus*, a species known to occur in endemic yellow fever zones.

Haemagogus splendens also found in Colombia has now been shown by the authors to be capable of transmitting yellow fever in the laboratory. The strain of virus used was originally isolated in a rhesus monkey by the bite of wild mosquitoes. It was then passaged once intracerebrally in white mice and reinoculated into a rhesus monkey, the dried serum of the latter serving as the source of virus for these experiments. Two species of monkeys, the saimiri and douroucouli, all trapped in the Villavicencio area, were used. The "extrinsic incubation period" has been between 14–16 days in mosquitoes kept at constant temperatures of 30°C. This is very close to the interval found necessary to obtain transmission with *H. spegazzinii falco* by BATES and ROCA-GARCÍA [this *Bulletin*, 1946, v. 43, 32].

The percentage of feeding mosquitoes who become infected depends directly on the amount of virus circulating in the blood stream of the monkey. A titre of 10^{-4} as tested in mice, seemed to be necessary to ensure virus being recovered from the feeding mosquitoes. *F. O. MacCallum.*

WADDELL, Mary B. & TAYLOR, R. M. **Studies on Cyclic Passage of Yellow Fever Virus in South American Mammals and Mosquitoes. II. Marmosets (***Callithrix penicillata* **and** *Leontocebus chrysomelas***) in combination with** *Aëdes aegypti*. *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 455–63, 2 figs.

The authors have been carrying out studies in Brazil similar to those described above by BATES and ROCA-GARCÍA in Colombia. They have been able to maintain a jungle strain of yellow fever virus by alternate passage through mosquitoes (*Aëdes aegypti*) and a species of marmoset (*Callithrix aurita*), as well as Cebus monkeys (*Cebus versutus*). They have isolated the virus on four separate occasions from captured marmosets (*Callithrix penicillata*). They here describe laboratory experiments which suggest the rôle in transmission of the virus, played by the two most common primates (*C. penicillata* and *Leontocebus chrysomelas*) found in the region where the virus was isolated. Field studies incriminated *Haemagogus* mosquitoes as the probable vector, but *A. aegypti* was used in laboratory as *H. spegazzinii* could not be reared in the laboratory. The virus could be maintained more readily by alternate passage through mosquitoes and marmosets than by direct syringe-passage from marmoset to marmoset.

The infection in *L. chrysomelas* was milder than in *C. penicillata* though all six animals circulated virus. Mosquitoes fed during the early stages of infection consistently contained virus, but mosquitoes feeding on the 7th day, and in one instance on the 5th day, following exposure of the animal failed to show virus after the period of incubation although virus was still circulating in diminished concentration at time of feeding.

These two marmosets apparently are the principal, if not the sole, vertebrate hosts of the virus in the area studied in South-Eastern Bahia State.

F. O. MacCallum.

BATES, M. & ROCA-GARCÍA, M. **Experiments with various Colombian Marsupials and Primates in Laboratory Cycles of Yellow Fever.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 437–53, 4 figs. & 2 diagrams. [27 refs.]

The extensive field studies of sylvatic yellow fever that have been carried out in Brazil and Colombia all indicate the virus is maintained in nature by constant mammal-mosquito passage, and that in many areas at least, the vector mosquito is *Haemagogus capricornii* or closely related species. The authors have previously shown [this *Bulletin*, 1946, v. 43, 32] that in the laboratory, this mosquito requires rather special conditions for infection, and an important condition is the amount of virus in circulation in the host mammal. It has also been shown that *Haemagogus* mosquitoes differ from *Aëdes aegypti* in infection behaviour and that virus strains differ in their behaviour in certain mammals, *e.g.* marmosets. The present paper is a continuation of studies carried out by the authors in Colombia on local mammals, local mosquitoes and local virus.

Only one of 11 attempts to infect *Haemagogus* on the brown-masked opossum (*Metachirus*) was successful, though 11 of 13 animals bitten by infected *Haemagogus* showed circulating virus. The woolly opossum (*Caluromys*) was much less susceptible. The authors consider these to be the two most susceptible of Colombian marsupials and it thus seems doubtful whether any of the local marsupials can play an important rôle in haemagogus cycles in nature.

It was easy to maintain cycles of infection with *Haemagogus* mosquitoes and saimiri or douroucouli monkeys or the marmoset (*Oedipomidas oedipus*). Attempts to infect the widow monkey (*Callicebus*) gave irregular results and the local capuchin (*Cebus fatuèllus*) in four experiments failed to circulate enough virus to infect haemagogus mosquitoes. Cebus monkeys in Villavicencio area frequently show positive sera and the authors think these may represent a " dead-end " in natural virus cycle.

Transmission may be shorter in nature than in the laboratory, so that one passage a month may be the maximum natural rate. This means that explosive epidemics such as are sometimes found in areas peripheral to regions where sylvatic yellow fever is endemic, might require several months to build up to the point where they are discovered. Human infections may lag months behind actual epizootic spread of virus. Virus is circulated in the monkeys 7–8 days at most but in mosquitoes for life, so that spread is more likely a function of mosquitoes than of mammals. *F. O. MacCallum.*

LAUTERBURG-BONJOUR, M. Ueber Gelbfieberschutzimpfungen. [**The Prevention of Yellow Fever.**] *Schweiz. med. Woch.* 1946, Nov. 23, v. 76, No. 47, 1206–10. [71 refs.]

A review of work on yellow fever prophylaxis.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

ELSDON-DEW, R., with the technical assistance of R. HORNER & D. A. CAMERON. **Some Aspects of Amoebiasis in Africans.** *South African Med. J.* 1946, Oct. 12 & 26, v. 20, Nos. 19 & 20, 580–87 ; 620–26, 12 charts. [198 refs.]

As a preliminary, the first three pages of this paper consist of a survey of a formidable number of papers [chiefly American] on the discovery and nomenclature of *Entamoeba histolytica*, its relation to amoebic dysentery, the probable

modes of its dissemination and entry into the individual, and the types and site of the intestinal lesions it may give rise to in man and in experimental animals. Embolic infection of the liver is stated, in general, to be comparatively common, with the liver more often than not winning the battle between the cytolytic activities of the parasite and the reparative activity of the host; in support of this view is adduced as evidence "the heavy fibrous capsule found in even the largest of abscesses" [this is a most unusual finding]. The literature on the strains of *E. histolytica* and on the possible multiplicity of species is summarized, as is that on the differing susceptibilities of natural and experimental hosts. The effect of diet and of concurrent bacterial infections on the intestinal infection is reviewed, and the rarer involvement of tissues elsewhere in the body is also dealt with. The difficulties in detecting the presence of the parasite are mentioned, and its geographical distribution is not neglected.

The more immediate purpose of the paper is to record the gravity of the problem of amoebiasis in the African in Natal and more particularly in Durban, and to this end data are given on this disease as encountered in the King Edward VIII Hospital, Durban, a 1,200-bed hospital which admitted totals of 33,018 and 34,284 patients in 1944 and in 1945 respectively. Stools from patients giving some clinical indication of dysentery were there examined as fresh film preparations; the examinations were made on three consecutive days, and it is estimated that between 65 and 70 per cent. of infections were detected by this means. Most persons harbouring *E. histolytica* were found to be passing amoebae, which were readily detected; cysts were more difficult to find, owing to the irregularity in their passage, and also in their distribution in the specimens. Faust's zinc sulphate concentration technique for cysts was adopted in the examination of over 1,000 specimens, and in a chart and a table the results obtained by direct examination and by the concentration technique are compared, the advantage lying with the latter. In further charts and tables are displayed the results of the examination for protozoa and helminths of 20,243 stools from Africans and 1,838 from Indians, and also the case-incidence of the various protozoa and helminth infestations detected in 4,852 Africans and 500 Indians. From these it can be seen that from 32·83 per cent. of the Africans and 38·00 per cent. of the Indians no parasites at all were recovered; that 27·51 per cent. of the Africans and 9·00 per cent. of the Indians harboured *E. histolytica*; and that most of the protozoal and helminth parasites commonly found in the stools of those living in the tropics were well represented, *Ascaris* being the most common (Africans 37·55 per cent., Indians 38·20 per cent.). In Indians *E. histolytica* gives rise to a chronic somewhat indefinite syndrome, akin to that found locally in Europeans, while in the African the disease is an acute fulminating one with severe diarrhoea and the passage of blood, mucus and pus containing very large numbers of amoebae; in these Africans the mortality is high. On culture, no specific concomitant infection with pathogenic bacteria was found to account for the severe symptoms in 50 Africans with acute amoebic dysentery.

The age-sex incidence of amoebiasis in Africans and Indians is tabulated, from 2 to 2½ times as many males as females being found infected in each group, the age group between 20 and 40 years being most affected (58·8 per cent. of cases). Some 42 cases were encountered in children under the age of 10 years. In Africans the main incidence of the acute disease was in the lower income groups, the better fed domestic servants being much less affected. In the native staff of the hospital acute amoebic dysentery is almost unknown, though chronic amoebiasis occurs. A spot map of the distribution of cases in Durban shows the greatest number of cases to occur in the Mayville district, which consists largely of shacks unsupplied by the essential services, water being obtained from communal standpipes or, when there is water in them, from local streams.

The population of Mayville is a mixed African and Indian one. In the Lamont Village area, where the population is purely African, acute amoebiasis was rare; other areas with a predominantly Indian population also had a low incidence of the disease—which suggests that a mixture of a susceptible [African] population with a non-susceptible carrier [Indian] population has some bearing on the high incidence in Mayville. Cases drawn from surrounding districts in Natal outside Durban show that acute amoebiasis occurs in all areas.

While inadequate sewage disposal accounts in part for the dissemination of the infection, it does not explain why the Indians living under conditions as insanitary as those found among the African population do not get severe amoebic dysentery.

A dietetic factor is probably involved, and support for this inference is derived from the increase in the infection during the war years. Serum specific gravity frequencies, determined by the copper sulphate method, in cases of amoebic dysentery and of non-amoebic dysentery, as compared with those found in normal controls taken from the well-fed hospital staff, showed a tendency to lowering of the protein factors. While cases of amoebic dysentery were all more or less deficient in protein, some cases of non-amoebic dysentery had protein levels in the higher range of normality. That both Africans and Indians are similarly exposed to faecal contamination of food is indicated by the comparable incidence of such helminths as *Ascaris* and *Trichuris*, but a difference in their diet is indicated by the relative absence of *Taenia* infection in the Indians. That the diet of the African is deficient, substantially consisting as it does of maize, is well known; and severe amoebiasis is known to be associated with a maize diet. Climate plays a part in the ease of transmission of the parasite and the severity of the disease resulting from its presence. From tables and charts it is shown that there is a demonstrable periodicity in the incidence of the disease, which attains its maximum in March and minimum in August, following, with a lag, the maxima and minima for temperature and rainfall.

The mortality of the disease, as shown by tables, was extraordinarily high (10·7 per cent. for all cases [? African]) despite early institutional treatment, and a common cause of death was perforation. Attempted treatment with high enemata of raw liver had to be abandoned owing to the shock caused.

A. R. D. Adams.

Ayadi, M. S. & El Kordy, M. I. **Cultivation of *Entamoeba histolytica* in Tomato Juice.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 214–18.

Halawani, A. & El Kordy, M. **Cultivation of *Entamoeba histolytica* in Hydatid Scolices Extract.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 211–13.

"1. A new fluid medium (made from an extract of dried hydatid scolices in Ringer's solution) for the cultivation of *E. histolytica* is described in the text.

"2. This scolices-medium has proved very efficacious for the cultivation of *E. histolytica* and for its maintenance in subcultures.

"3. It appears according to our experience so far that *E. histolytica* requires for its growth a very small amount of protein, rice-starch, micro-organisms and adjustment of the pH of the medium. These requirements are present in the dried scolices-extract-medium."

Bourova, L. F. Étude expérimentale des amibes du type *histolytica* chez les singes inférieurs. [**Experimental Study of** *histolytica*-**like Amoebae in Monkeys.**] *Ann. Parasit. Humaine et Comparée.* 1946, v. 21, Nos. 3/4, 97–118, 7 figs.

Working in the monkey park at Soukhoum in the Caucasus the author has found that certain monkeys harbour amoebae of the *Entamoeba histolytica* type and that the feeding of cysts in milk to kittens frequently results in amoebic infections which in many cases are of the dysenteric type. Among 18 attempts to infect kittens with the amoebae from a *Cynocephalus hamadrias* 8 were successful; of 11 attempts to infect with the amoebae of a *C. anubis* 5 were successful, while of 25 attempts with amoebae from three *Macacus nemestrinus*, 10 were successful. Amoebae from two other *C. hamadrias* failed to infect kittens in 9 attempts. In one of the infections produced by amoebae from *C. hamadrias* only small amoebae 5 to 3 μ in diameter were found. Yet when this strain was passed to another kitten, presumably by rectal inoculation, an acute amoebic dysentery associated with the usual large amoebae developed. The author concludes that the amoebae of the monkeys behave as regards pathogenicity to kittens exactly as do *E. histolytica* from human beings.

C. M. Wenyon.

Adler, S. & Foner, Ann. **The Lytic Action of Normal Faeces on the Vegetative Form of** *Entamoeba histolytica. Harefuah.* Jerusalem. 1946, May 15, v. 30, No. 10. [In Hebrew 237–9. English summary 239.]

Having been called upon to arrange demonstrations of *Entamoeba histolytica* in stools, the authors prepared material by mixing faeces with rich cultures of the amoeba. It was noted that within half an hour the amoebae had diminished to such an extent that it was difficult to demonstrate them. It was evident that they were being destroyed by the faecal material. The phenomenon was tested more accurately by mixing known concentrations of amoebae with known quantities of faeces, keeping the mixture at 37°C. and making counts at intervals. It was clear from these quantitative investigations that the addition of vegetative *E. histolytica* to normal faeces is followed by a rapid destruction of the amoebae. The greater part of this destruction occurs within two minutes. In one case the contact with faeces induced encystment of the amoebae. With certain pathological stools the destruction was less rapid, while with stools of several cases of amoebic dysentery the amoebae appeared to survive for longer periods.

C. M. Wenyon.

Jones, W. R. **The Experimental Infection of Rats with** *Entamoeba histolytica*; **with a Method for evaluating the Anti-Amoebic Properties of New Compounds.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 130–40, 7 figs. on 2 pls. & 3 text figs. [16 refs.]

Earlier attempts to infect rats with *E. histolytica* having given very uncertain results, the author investigated the possibility of improving these by modified techniques. Direct injection of culture material rectally or intracaecally after laparatomy into 46 three-month-old rats failed entirely, though purging, starving, modification of diet and occlusion of the anus were tried. Better results were obtained by first establishing an infection in kittens by rectal injection of culture and then inoculating the dysenteric stools of the kittens intracaecally into rats. Not only were the rats parasitized by *E. histolytica* but at autopsy some showed marked inflammation and even ulceration of the caecum, while section of the tissues revealed extensive invasion of the gut wall. In attempts to produce infection by injection of the same material rectally only

two of eleven became infected but these had ulceration of the caecum when examined after 28 days. A series of photographs shows the external appearance of the inflamed caeca of four rats and the microscopic changes which occur in the invaded intestine.

The various degrees of infection were allotted numbers from 0 to 5, so that the extent of infection in any group of rats could be given an average number indicating the average degree of infection (A.D.I.). It was found that this diminished progressively as the average weight of groups of rats increased, the best results being obtained in the 20 to 33 gramme (3–4 weeks old) group, which gave an A.D.I. of about 2·5–3·5. This method of recording infections afforded a means of estimating the effect of possible chemotherapeutic agents.

The normal course of the infection was studied in several groups of rats by examination of the caecum and large intestine post mortem. This showed that infection was at its height in 3–6 days and that it might gradually disappear entirely from the majority of rats in a group during the 7 to 28-day period. Ulceration might be evident within 24 hours. Cysts were occasionally detected during the 14 to 28-day period. Only a small proportion of the rats showed obvious clinical signs of infection, such as dysenteric stools, while certain rats with massive ulceration of the caecum appeared quite normal. The infection in the rats is not readily detected by direct microscopic examination or culture of the faeces.

It was later found that if cultures of *E. histolytica* were mixed with mucin the mixture injected intracaecally produced infections, as did the kitten material. With this mixture a standard test for chemotherapeutic agents was worked out. Five groups of 12 rats are infected with a mucin culture mixture containing one million amoebae per cc. Each rat receives intracaecally 0·2 cc. of the mixture. This operation can be carried out with the aid of an assistant at the rate of 50 to 55 rats an hour. Four of the groups are dosed with the drug 24 hours after operation. One group serves as the control. Six days after operation the rats are killed and a detailed examination made and the A.D.I. calculated for each group. The significance is assessed by a statistical formula and reference to a graph correlating the standard deviation and average degree of infection. The interesting observation was made that different strains of *E. histolytica* do not respond in the same way to emetine hydrochloride. In the investigation it has been found that the drugs which are used for the treatment of amoebic dysentery in man—emetine, chiniofon, carbarsone, stovarsol—show up favourably, so that there is a hope that the test employed may lead to improved methods of treatment. Penicillin only gave some indication of activity when administered in large doses every three hours. *C. M. Wenyon.*

BROWN, A. F. **Amoebiasis.** [Correspondence.] *Brit. Med. J.* 1946, Nov. 30, 838.

This letter draws attention to the possible spread of amoebiasis in Great Britain where rural sanitation still exists and to the possible infection of food by cyst-passers. The writer is impressed with the provocative action of emetine—gr. ½–1 by injection nearly always produces cysts the next morning. They usually contain one or two nuclei which indicates that they wish to find a new host in a hurry. [The evidence for these statements is flimsy indeed.]

P. Manson-Bahr.

MORTON, T. C. **Diagnosis of Chronic Dysentery in Service Personnel. Analysis of 1,000 Sigmoidoscopies.** *Brit. Med. J.* 1946, Dec. 14, 890–93.

A thousand sigmoidoscopic examinations were performed on Service patients invalided with a diagnosis of chronic amoebic or bacillary dysentery.

Sigmoidoscopy was carried out in the knee-elbow position without an anaesthetic. The new type sigmoidoscopes were employed which take a 6-volt car bulb light, giving excellent illumination with a magnifying ×4 eyepiece. No preliminary washout within six hours must be given, because it renders the mucosa hyperaemic and identification of the "raised crateriform pits" impossible. The following preparation is recommended: A light lunch and tea is followed by a washout with tap water at 8.0 p.m. No supper is given that night. No breakfast is allowed on the morning of the examination. The bladder should be empty. A scraping and swab from any suspicious area should be mounted and examined without delay for *E. histolytica*. A warmed plate of Hynes's modification of Leifson's desoxycholate citrate medium should be inoculated and cultured. Any faeces adherent to bowel wall are examined for *E. histolytica*.

Among 1,000 patients sigmoidoscoped, only 513 gave positive findings. In the remaining 487 sigmoidoscopy and laboratory investigations were negative. The findings were: amoebiasis 215 (mixed amoebic and bacillary 11); bacillary dysentery 52 (Shiga 2, Schmitz 3, Sonne 4, Flexner 43). In approximately 20 per cent. of 215 amoebic cases, sigmoidoscopic appearances were normal. In bacillary dysentery, out of 52 positive findings the appearances were normal in 9.

Amoebic ulcers conformed to text-book descriptions, but five amoebomata were encountered in unrecognized amoebiasis.

Raised crateriform pits pathognomonic of quiescent amoebiasis were present in 169 patients, and in 78 of them *E. histolytica* was found in the faeces. The pits are circular in shape, 1–2 mm. in diameter, and raised 1 mm. above the surrounding surface. It is usually impossible to find *E. histolytica* in scrapings taken directly from the pits. Cases showing the characteristic appearance should be treated, even if the stools are negative. In a small number of cases in which these pits have been seen after treatment relapses occurred sooner or later. They must not be confused with the pseudocystic "sago-grain" follicles which sometimes follow bacillary dysentery.

The essential points of amoebic pits are their regularity, concentric appearance and the presence of the circular lip of the volcano surrounding a slightly depressed crater. Raised lymphoid follicles must also be distinguished; in them the central depression is absent. When the pits are still active, gentle swabbing gives rise to petechial bleeding which is suggestive and can be confirmed by creating an artificial diarrhoea by means of salts in order to provoke the appearance of *E. histolytica* in the faeces.

Depressed pits were seen in 126 cases and *E. histolytica* was found in 20 of them. It is explained that active lesions are present at a higher level of the colon in the negative cases. "Pitting" in healed bacillary dysentery cases is more irregular in shape and size, is tessellated and lacks the circular uniformity of amoebic "pitting". Fifty-eight symptomless cyst-carriers were detected and in 16 only these typical pits were seen. It is assumed that in the remainder, lesions were out of range of the sigmoidoscope.

Ten cases of amoebic liver abscess occurred in this series. In two, spontaneous rupture into the peritoneum was diagnosed at operation and in both the abscess was situated in the left lobe. In a total of 60 cases of amoebic hepatitis, four only developed in England. A moderate leucocytosis was found to be of value. The lowest white cell count was 14,200 per cmm. and the highest 27,500. The average was 15,800 with 75 per cent. polymorphonuclears.

Amoeboma is a hyperplastic localized tissue reaction, chiefly affecting the submucosa, which is infiltrated with lymphocytes, histiocytes and plasma cells, together with *E. histolytica* in localized clusters. It is relatively rare.

Five cases were detected, and in four the growth was in range of the sigmoidoscope. The usual symptoms evoked are intermittent attacks of diarrhoea and constipation. Blood is occasionally passed and may be attributed to concurrent haemorrhoids. Diagnosis by scrapings is the best and surest method. Stenosis of the bowel is often present, but after a course of emetine and penicillin the growth melts away.

Stricture of the rectum, as a remote complication of amoebic dysentery, rarely occurs. One case in the series was open to some doubt. Although proven to be amoebic, the actual stricture was a sequel to the passage of a large slough *per rectum*, which probably resulted from massive secondary bacterial invasion.

Amoebiasis simulating appendicitis occurred in 4 cases in which acute amoebic dysentery ensued within 48 hours of operation. Perforation of an amoebic ulcer in the caecum occurred once and was successfully closed by operation.

Six cases of adenocarcinoma of the rectum or sigmoid were seen. In only one patient had the diagnosis been arrived at overseas, though, ironically, he developed amoebic hepatitis whilst convalescing from his colostomy. The ages of these patients were higher (31–43 years) than the mean age for the group (26 years). In three cases the growth was within reach of the examining finger and the pronounced induration suggested malignant disease rather than amoeboma.

Lambliasis. Cysts or free forms were found in only 40 cases, in 18 no other cause could be found for the diarrhoea and symptoms disappeared after mepacrine therapy. The surprisingly low incidence is ascribed to repeated therapeutic courses of mepacrine for malaria.

Bacillary dysentery. The large number in which the causative organisms were cultured is ascribed to the extreme selectivity of modern media. In 31 out of 52 cases, the diagnosis had not been made overseas and the majority had received amoebic treatment without benefit.

The sigmoidoscopic appearances were :—

(1) generalized hyperaemia with excess of mucus.

(2) generalized hyperaemia with tubular stenosed lumen, with a granular appearance, bleeding readily on instrumentation. The prognosis is poor.

(3) superficial oval or circular ulcers up to 1 cm. in diameter ; the bowel wall distends readily and there may be no inflammation in the intervening mucosa. One such case mimicked an amoebic ulcer very closely. *Sh. flexneri* VI was isolated after the third attempt.

(4) a puzzling appearance, characteristic of bacillary dysentery is a pseudocystic condition arising from the occlusion of the crypts of Lieberkühn. There are " sago grain " elevations 1–3 mm. in diameter scattered over the mucosa. On rupture there exudes clear or blood-stained mucus from which the causative organism can be isolated. From one such case, who was invalided from Italy with a diagnosis of polyposis, *Sh. flexneri* III was isolated.

Complications of bacillary dysentery were infrequent because of sulphaguanidine therapy. Two cases showed a general narrowing of the rectum, associated with granular, hyperaemic, easily traumatized mucosa. The prognosis is poor. Two cases of arthritis of the ankle joint were noted and both recovered.

Seven cases of *ulcerative colitis* were diagnosed, in which laboratory investigations and agglutination tests were negative. The association with bacillary dysentery was not confirmed.

Four cases of *hyperplastic colitis* were seen in which the sigmoidoscopic appearances were deep, greyish depressions, the site of healed ulcers, surrounded by overhanging hypertrophied bridges of red mucosa. The mucosa bridged the depressions and in one instance divided the lumen into two. The symptoms

were pain and bleeding following constipation ; and in one case it was necessary to divide a band of mucosa. Agglutinations for *Sh. flexneri* were positive 1/50 in one case. It is probable that this condition is an excessive healing response to extensive ulceration of bacillary dysentery.

Post-dysenteric colitis. In 16 cases, residual colitis persisted after treatment. One patient had to be invalided ; in the others, a slow gradual improvement has taken place.

The sprue syndrome. Numerous patients have been invalided with a diagnosis of sprue or para-sprue. In some cases, the syndrome has developed within four months of arrival in India. Eighty cases were sigmoidoscoped and investigated. It was found that 46 per cent. were found to be harbouring pathogenic intestinal protozoa or bacteria and that, when these were eradicated, the sprue symptoms responded to the routine orthodox treatment for sprue. This series is compared with a larger one of 152 similar cases investigated in R.A.F. hospitals in England, in which routine sigmoidoscopy was omitted. The incidence of pathogenic protozoa or bacteria in this larger series was 4·5 per cent., indicating the value of sigmoidoscopic examination in sprue.

P. Manson-Bahr.

Warshawsky, H., Nolan, D. E. & Abramson, W. **Hepatic Complications of Amebiasis.** *New England J. of Med.* 1946, Nov. 7, v. 235, No. 19, 678–81.

Report of four cases.

Lewis, R. A. **Enteric Infections and their Sequelae.** *New England J. of Med.* 1946, Oct. 17, v. 235, No. 16, 571–81. [12 refs.]

Acute dysenteric diseases have been studied in many overseas hospitals, but follow-up studies are scarce. The cases referred to in this paper were observed in a U.S. Army general hospital during the latter half of 1945. All patients were allowed to go home for 30–60 days before a final check-up, so as to provide a sufficiently long follow-up period after treatment. Practically all were examined by sigmoidoscopy. Amoebiasis was diagnosed in a quarter of the cases and the number classified as carriers of *E. histolytica* was larger in the United States than overseas.

The incidence of hookworm was identical, but more were found to have strongyloidiasis than overseas. Of the 105 only two had never been overseas, and the greater majority had been in the Pacific. Some with no symptoms and no pathological findings, other than eosinophilia and ova in the stools, were classified as carriers.

In amoebiasis, strongyloidiasis and schistosomiasis there were more patients with symptoms than there were carriers.

Carriers of *E. histolytica* should be treated to prevent subsequent development of dysentery. The importance of sigmoidoscopic examination and the collection of purged stools in diagnosis is emphasized, as well as the need for early clinical diagnosis of amoebic hepatitis and for prompt emetine treatment.

Tissue invasion by *E. histolytica*, which can usually be verified by positive complement fixation tests, may produce rectal stricture and appendicitis as well as granulomata. Patients with amoebic dysentery with rectal involvement—detected either by proctoscopy or presence of blood in faeces—should be treated by retention enemata. Vioform suspensions are non-irritating and form convenient enemata in treatment, but it is advisable to combine these with an oral course of the drug, thus obviating the use of chiniofon and carbarsone which may aggravate diarrhoea.

Ulcerative colitis, the author believes, may develop after severe amoebic as well as after bacillary dysentery. A large proportion of cases regarded as

unclassified dysentery will be found to have steatorrhoea on analysis of the 24-hour stool for fat. Most of them correspond to early stages in the development of sprue and despite loss of weight there may be no sign of vitamin deficiency. These patients respond well to a diet strictly limited in fat and high in protein and carbohydrate. *P. Manson-Bahr.*

HOLLER, G. & ZAJITSCHEK, R. Vorschlag einer Methode zur Entkeimung von Amöben- und Bazillenträgern. [**A Method for sterilizing Amoebic- and Bacillary Dysentery Carriers.**] *Wien. med. Woch.* 1946, Jan. 15, v. 96, Nos. 1/4, 2–7.

In amoebic dysentery, bacillary dysentery and typhoid fever small numbers of the causative organisms give rise to infection on being swallowed, and subsequently large numbers of the organisms are voided in the excreta. During war these diseases flourish and are disseminated by numerous carriers. This paper is concerned with the means of sterilization of such carriers.

1. An amoebic dysenteric infection can only persist in a damaged intestine. The usual method of eradicating such an infection is the administration of drugs to destroy the amoebae. The restoration of the bowel to normal will, however, achieve the same result. To achieve this healing of the bowel, the treatment advocated by Eppinger was adopted. Eppinger's treatment for colitis consisted of the introduction of 5–8 per cent. glucose solution by rectal drip to a total volume of 1 litre over a period of 2–3 hours. This cleanses the bowel wall of its inflammatory exudate and increases healing by promoting an increased blood supply to the area. Six cases of chronic amoebic dysentery, previously repeatedly treated unsuccessfully with a variety of drugs in various combinations by the authors and by others, were given rectal injections of hypertonic glucose solution (10 to 20 per cent.), as outlined above, daily for periods up to 10 days ; in some cases, these were repeated on a second or a third occasion, at times concurrently with some of the usual anti-amoebic drugs. In every one of the six cases, the *Entamoeba histolytica* infection of the gut was eradicated by the treatment.

A carrier of a bacillary dysenteric infection of the bowel remains chronically ill with bacillary dysentery, and from time to time passes stools containing blood and mucus with many bacilli. In such cases, chemotherapeutic remedies (Eluedron, Eubasin, Cibazol, etc.) will rapidly eradicate the specific bacillary infection. These drugs should be used to this end, and healing of the bowel wall should then be ensured by hypertonic glucose enemata.

2. In the case of typhoid carriers, infection of the biliary tracts and gall-bladder results in the passage of organisms from these sites in the stools. Infection of the pancreas, of the villi of the small intestine, and of the appendix also contributes organisms to the stool. These carriers are intestinal excreters of the bacilli ; they may be temporary or permanent, the former being convalescent from an attack of the disease and excreting bacilli for not more than three months. Urinary excretion of bacilli occurs similarly.

There is no specific chemotherapeutic remedy for the typhoid and paratyphoid infections, but HOLLER, MATHIS and ORTNER found nitroacridine (Bayer 3582), in doses of a heaped teaspoonful six-hourly, to clear the blood of bacilli by the tenth dose in all but one of 150 cases. In this single case, a second course of the drug achieved the desired result. Nevertheless, bacilli could be recovered after this treatment from the urine and faeces of these cases, but no chronic carrier state developed in any of them. The observation has been confirmed by the treatment of a further 50 cases ; and again, with one exception, no bacilli could be found in the stools one month after the fever, and none were found in the urine at the end of the acute stage.

Temporary carriers are numerous after an attack of enteric, and chronic intestinal carriers develop in 1–10 per cent. of cases ; chronic urinary carriers are much less numerous, but are very persistent (70 years in one case). Among 317 cases of enteric seen by the authors during the previous ten years 11 became chronic urinary and 32 chronic intestinal carriers. In the 200 cases treated with nitroacridine (Bayer 3582) not a single case became a chronic carrier. Sixteen proven chronic intestinal carriers were treated with the drug and all but two were sterilized of their infections ; these two resisted further repeated attempts at sterilization. Experience has indicated that nitroacridine (Bayer 3582) readily sterilizes urinary carriers.

As rectal injections of hypertonic glucose solution would not reach the sites of lodgement of bacilli in intestinal carriers of enteric, the authors resorted to irrigation through a duodenal tube (1 litre of 10–20 per cent. glucose solution in 3 hours on alternate days). This method has proved of value in the treatment of cholangitis, cholecystitis and cholelithiasis, probably as a result of mechanical increase in bile secretion. Duodenal irrigation alternating daily with rectal irrigation for 10 days was tried in intestinal carriers of enteric. Details of six representative cases are recorded, four of them temporary (convalescent) carriers and two chronic carriers ; this treatment either alone or in combination with nitroacridine (Bayer 3582) treatment ensured sterilization of the infection in all six.

Alimentary carriers of enteric are apparently healthy persons, with no clinical symptoms of disease, encountered in typhoid endemic areas who have transient infections of the intestinal contents. These persons swallow the bacilli and pass them in the stools without necessarily themselves becoming infected with them. They may, however, become chronic carriers, or they may develop acute typhoid. A chronic carrier, also, may develop acute typhoid ; two cases are cited to illustrate this. *A. R. D. Adams.*

Mandoul, R. & Pautrizel, R. Régime alimentaire, chimisme intestinal et parasitisme. [**Diet, Intestinal Chemistry and Parasitism.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 222–6.

The authors refer to the recent article by Chorine and Tanguy [this *Bulletin*, 1947, v. 44, 211] who showed that during the war the incidence of intestinal protozoal infections in Paris has increased considerably. They attributed this to the enforced vegetarian diet. The authors of the present paper have found a similar increase in Bordeaux. However, they hold that the direct cause is the resulting increase in the ammonia and the amino-acids, increases which are not always disclosed by the *p*H. These increases are due to the putrefaction set up by the proteolytic bacteria, which in their turn are favoured by the hypersecretion of mucus and nucleoproteid resulting from the excessive development of the saccharolytic bacteria and the consequent acidity. *C. M. Wenyon.*

Sarrouy, C. & Combe, P. Notes sur les syndromes digestifs graves d'été du nourrisson en Algérie et leur traitement d'urgence. [**The Treatment of Acute Summer Digestive Disturbances in Algeria.**] *Algérie Méd.* 1946, July–Aug., No. 4, 307–20.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

HADDAD, C., SHEIBAN, A. & BUDEIR, R. **Louse Borne Relapsing Fever in Haifa.** *J. Palestine Arab Med. Ass.* 1946, Nov., v. 2, No. 1, 8–14. [12 refs.]

"The symptoms, complications and treatment of 200 cases of louse-borne relapsing fever seen in Haifa are described. A comparison with the epidemic which raged during the first World War (1914–1919) points to the fact that the present epidemic is of a lighter character. In a future paper it is intended to describe the cases of tick-borne recurrent fever which came under our observation in Haifa."

FISCHER, Isadore. **Penicillin Therapy in Relapsing Fever. Report of Case.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 483–8, 1 fig.

VAN RIEL, J. Le foyer centro-africain de leptospirose. (Contribution au problème de l'unité ou de la pluralité des leptospires du type. *L icterohaemorrhagiae.*) [**A Central-African Focus of Leptospirosis. A Contribution to the Unity or Plurality of Leptospiroses of the** *L. icterohaemorrhagiae* **Type.**] *Ann. Soc. Belge de Méd. Trop.* 1946, Sept., v. 26, No. 3, 197–313. [231 refs.]

A valuable study of the complex problem of the unity or plurality of Leptospiroses, based mainly on the author's observations on local strains of the disease in the neighbourhood of Lake Kivu, Belgian Congo.

Weil's Disease, infectious jaundice with relapses, is stated to be really only one of the types, and not the most frequent, of a very variable infection. In the region of Lake Kivu a wide range of clinical varieties was found, including anicteric forms and also the curious meningitic type of the disease. The various symptoms seem to depend on which of three parts of the body—liver, kidney, or meninges—are attacked. In addition, inapparent cases have been discovered in sections of the population specially exposed to infection.

According to the plurality theory, strongly advocated by Schüffner, there existed in 1938 at least 19 antigenically autonomous species of *Leptospira*, 14 human and 5 exclusively animal. These were supposed to differ in their geographical range, clinical symptoms, animal hosts, epidemiology, and, finally, in their pathogenicity to guineapigs. The author points out, however, the very slender evidence on which many of these so-called species are based. Thus only 24 cases of "Andaman A" have been identified in those islands; 80 cases of "Pomona" in Australia; and only 22 cases of "*Canicola*" in man. "Sejrö" Leptospirosis has been found 3 times in Denmark and 13 times in Italy. Yet these few cases have been made the basis of conclusions as to the virulence and the icterogenic or non-icterogenic character of the infection.

The author then proceeds to give a detailed account of his own observations on the various strains of Leptospirosis occurring in the neighbourhood of Lake Kivu, Belgian Congo. Twenty-one strains were isolated, 18 from human patients, 2 from a rodent, *Arvicanthis abyssinicus*, and one from water. Using the agglutination-lysis reaction and also saturation of antibodies, these strains were analysed for their antigenic properties, and it was found possible to divide them into 8 groups. The first resembled *L. grippo-typhosa*; the second, *L. bataviae*; the third, the "Benjamin" strain from the Dutch East Indies, but also reacted with other strains; the fourth and fifth were each new types; and finally the three last groups seemed to be related to both *L. icterohaemorrhagiae* and *L. canicola*.

The clinical symptoms are next considered and it is shown that in the Congo there is no correlation between the aetiological agent and the clinical type.

Attention is also called to similar discrepancies in other parts of the world. Concerning geographical distribution, 31 serological types are listed in tabular form, together with the countries in which they occur. This distribution can be seen to follow no obvious rule, for one strain may be recorded from the Belgian Congo, Europe and the Andaman Islands; another from the Belgian Congo and Indonesia, etc.

The part played by animal reservoirs is then criticized and attention called to the marked lack of correlation between murine and human endemicity. Epidemiology is next considered and the incidence of the disease shown to be consistent with the view that it is essentially an occupational hazard, and that in the great majority of cases the infection is derived from water. The relation between the saprophytic *L. biflexa* and the pathogenic spirochaetes which have been isolated from water or mud, is reviewed. Finally pathogenicity in guinea pigs is considered and the author's results do not confirm the view that each serological type of *Leptospira* has a characteristic virulence in this animal. The pathogenicity varies according to the method of infection, age of culture, and many other factors; also the receptivity of different races of guineapigs is variable. For example, in Capetown the author was unable to infect the guineapigs at the local Medical School with three strains that had given lethalities of 37, 69 and 92 per cent. respectively in the Belgian Congo guineapigs. The so-called *L. grippo-typhosa* is generally stated to be hardly pathogenic and feebly icteric in the guineapig, but in the author's hands gave a high mortality with frequent jaundice.

The author concludes that at present in addition to *L. biflexa*, the only well-established species of *Leptospira* are *L. icterohaemorrhagiae*, and possibly *L. hebdomadis* or some allied species, but not *L. canicola*.

[This interesting monograph should be read in its entirety by those interested in the subject, as it summarizes the evidence in support of the water origin of Leptospirosis, which has received too little attention in recent years.]

E. Hindle.

Jackson, H. & Oleesky, S. **An Unusual Case of Weil's Disease.** *Brit. Med. J.* 1946, Nov. 30, 813–14.

LEPROSY.

Moiser, B. **Leprosy: a New Outlook.** *East African Med. J.* 1946, Oct., v. 23, No. 10, 295–300.

This paper deals with the same work as one already reviewed [see this *Bulletin*, 1946, v. 43, 454]. The author thinks that if the name of Hansen's disease is substituted for leprosy "you have got rid of the dread of the disease." He can find no evidence that either compulsory or voluntary segregation has ever reduced leprosy, but he advocates the latter. He states that the disease is a rural, family and home disease, but he thinks it "a complete fallacy to say that long continued, close, intimate contact is necessary for the transmission from the diseased to the healthy," and he knows of no "facts that have ever been brought forward to prove this." He has therefore sought for a new outlook and thinks he has found it through the observations recorded in his previous paper that cockroaches, both in leprosy hospitals and after feeding the insects on leprosy patients (but also in those found in villages with no cases of leprosy) may show in the intestinal canal oval acid-fast staining bodies which he assumes to be a stage of a pleomorphic lepra bacillus, and which may be found in the

droppings of cockroaches up to at least sixteen months. He states that these insects bite man " voraciously ", so he suggests that they transmit leprosy to mankind. Contrary to the findings of many earlier workers, he has not found acid-fast organisms in other insects, such as fleas, bed bugs or ticks. He advocates further research on these lines with the aid of a mobile laboratory. Definite proof of his hypothesis can only be obtained by experiments on man, the validity of which he is doubtful about. *L. Rogers.*

FLOCH, H. & DE LAJUDIE, P. Sur la lèpre en Guyane Française. I. Généralités. Répartition par âge. Dépistage. Contamination. [**Leprosy in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 131.* 1946, July, 6 pp. [10 refs.]

The author quotes data of the number of leprosy cases reported at different times in this French Colony from 1743 onwards. During the period from 1886 to 1937 the number of known cases increased from 100 to 200 to 609 and those among the penal element increased from 24 in 1897 to 130 seen from 1924 to 1928. Since the formation of the Institut Pasteur in the colony in 1914 more attention has been paid to leprosy and from 1925 to 1946, 1,447 cases have been recorded, and in the last-named year 1,131 cases were known against 677 at the end of 1938. That makes 5·1 per cent. of the estimated population of 22,000, to which must be added an estimated 300 cases to bring the percentage up to 6·5 per cent. The age incidence shows 44·3 per cent. up to the age of 15 years and 64 per cent. up to the age of 25. The largest proportions were at the ages of 6 to 10 among the children, many of which were detected by the examination of schools, and favourable results have followed the removal of such cases. Conditions under which infections occurred are most commonly family contaminations, and no evidence of the disease being hereditary was met with ; school infections were also frequent. Neuromacular cases were the most common form. *L. Rogers.*

MONTEL, R. & GIROUD, P. Affinités tinctoriales du bacille de Stefansky. (Méthode de Macchiavello.). [**Staining Reactions of Stefansky's Bacillus.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 248–50.

The following is a translation of the authors' summary.

In smears and frozen sections of rat lepromata, it was possible to distinguish two different morphological forms of Stefansky's bacillus, when the preparations were stained by Macchiavello's method without previous fixation : in one form, the organisms were unstained, refractile and in very large numbers : the others were much smaller, stained a ruby-red colour, were slender and very scanty.

These observations confirm those already made by one of us regarding Hansen's bacillus (*Mycobacterium leprae*) in the blood of leprosy patients. [See also this *Bulletin*, 1946, v. 43, 1152 *bis*.] *H. J. O'D. Burke-Gaffney.*

FURTADO, J. J. Da possível enzima segregada pelo " Mycobacterium leprae." [**A Possible Enzyme separated from** *M. leprae*.] *Publicações Farmacêuticas.* São Paulo. 1946, July, v. 12, No. 45, 15, 17–19. [19 refs.]

COCHRANE, R. G., MENON, K. P. & PANDIT, C. G. **A Further Note on Inoculation of Monkeys with Human Leprosy Material after Splenectomy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 88–97.

The authors have previously reported on seven monkeys inoculated with leprous material after splenectomy, with possible evidence of dissemination of

the infection in one; a failure they attribute to individual variability of resistance. They now report on sixteen further inoculations of monkeys with the following results. In Series A, three splenectomized monkeys were inoculated with leprous material on several occasions. No general dissemination of the infection was obtained. In Series B, three monkeys were splenectomized and inoculated with leprosy material and also fed on *Colocasia antiquorum*, on the hypothesis (which recent work has not confirmed) that such a diet predisposes to leprosy infection. In one an organism, considered not to be that of leprosy, developed, which it is thought had become pathogenic. Two of the animals also developed an erythematous rash. No dissemination of infection was found in any of these animals. In Series C, India ink was first injected to block the reticulo-endothelial system in three monkeys, but again no disseminated infection was produced. The interesting observation was made that all the animals, except those in which India ink was injected, tended to develop strong positive lepromin reactions after the third inoculation. *L. Rogers.*

COCHRANE, R. G. & RAMANUJAIN, K. **Inoculation of Monkeys with Human Leprosy Material.** *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 98–100, 3 figs. on 1 pl.

In this further paper the whole of the 38 inoculation experiments on monkeys during six years' work are summarized and the most important details shown in convenient tabular form. The lepromin reactions mentioned in the preceding abstract are also tabulated. It is suggested that *M. leprae* cannot parasitize the reticulo-endothelial system unless it multiplies in the corium of the skin; so blocking that system would not result in the development of progressive leprosy. The authors also conclude that a positive lepromin reaction could only be obtained in an animal after a primary focus had been established, such as by the intra-abdominal implantation of a nodule as was done in many of these experiments. They also suggest that in tuberculoid leprosy, the formation of epitheloid foci result in anchoring the bacilli and preventing their dissemination throughout the reticulo-endothelial system. Work will be continued with a view to breaking down the tissue defence reaction and to obtain disseminated infections. *L. Rogers.*

HANKS, J. H. **The Fate of the Bacilli in Incubated Lepromatous Tissues and the Question of Microscopic Growth.** *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 9–24. [16 refs.]

This is an important study of the difficult question as to whether lepra bacilli multiply in tissue cultures or not. Many have claimed that the bacilli multiply on media inoculated with small fragments of leprous tissues, which may contain so many organisms as apparently to form almost one-third of the area in stained sections, and probably constitute 20 per cent. of a richly infected leproma. Thus a ten-fold increase in the number of the bacilli should double the size of the implanted tissue. Quantitative estimations of the bacilli have therefore been made in incubated lepromatous tissues by methods which should detect with certainty a two-fold increase of the organisms. After control counts had been made, 2 mm. cubes of lepromatous tissues, previously tested for their sterility, have been incubated on culture media in tubes or flasks of various culture media and under varying conditions which have been reported as favourable to cultures. After various periods of time, estimations of the number of bacilli in the tissue cubes have been made with the greatest care, for details of which the original paper should be consulted.

The results of the tests are shown in tables with regard to four liquid media, namely : (1) liver infusion hormone glycerol agar in air ; (2) the same in a gas mixture of 10 per cent. CO_2 and 40 per cent. O_2 ; (3) serum, serum digest, Long's medium and 929 *p*H, plus the gas mixture ; and (4) peptic globulin digest, Long's medium, 929 *p*H and yeast extract ; gas mixture. Incubation was carried on for three to six months, but no definite increase in the number of the lepra bacilli could be demonstrated. In two more experiments with solid media, similar negative results were obtained. In two further tests, the liquid media were renewed periodically, also with negative results. The disintegration of tissue cells during incubation must release many bacilli ; this may produce an apparent increase of bacilli in smears made from incubated tissues as compared with fresh ones, and so lead to a false impression that the bacilli have multiplied. On several occasions, what appeared to be minute colonies were found microscopically to be small collections of lipoid material and not bacilli. In the present experiments, when the tissues were completely disintegrated and suspended before estimating the number of the bacilli recoverable from the tissues, it became evident that growth did not occur. *L. Rogers.*

DHARMENDRA & SEN, N. R. **Study of Leprosy in a Family.** *Leprosy in India.* 1946, Apr., v. 18, No. 2, 54–7.

The authors met with five early neural cases of leprosy in one family who attended the leprosy department of the Calcutta School of Tropical Medicine. On visiting their home two more similar cases were found, making seven neural cases among a family of 28 belonging to three generations. The absence of any infective lepromatous cases led to their making further inquiries, which resulted in finding that the family had come from Rangoon during the war, where they had been on very intimate terms with another family living opposite to them, among whom a few cases, apparently of a lepromatous type, were present, from whom the infection was probably derived. Lepromin tests were carried out in 26 of the 28 members of the Calcutta family with positive results in 25. This showed high resisting powers, which is in accordance with only neural cases having developed. *L. Rogers.*

DHARMENDRA & SANTRA, I. **A Study of the Course of the Disease in Leprosy.** *Leprosy in India.* 1946, Apr., v. 18, No. 2, 43–50.

This paper records the findings of a survey of 248 cases observed for ten years in the area of the Bankura leprosy centre and 88 cases seen for at least five years before death or disappearance. Only one-fourth of them were treated irregularly at clinics, with apparently less success than the untreated. At an early survey, only 26 per cent. were lepromatous and remaining nerve cases were mild in type. After the famine of 1943 the proportion of lepromatous cases fell to 15 per cent. owing to deaths, but the neural cases increased. Among 268 neural cases definite improvement or complete subsidence occurred in over 40 per cent. ; only 26 per cent. became worse, including 2·5 per cent. who became lepromatous ; all of these were macular with negative lepromin reactions, the prognostic value of which is confirmed. *L. Rogers.*

RADNA, R. Sur l'évolution de certains cas de lèpre neuromaculeuse. [**The Evolution of certain Cases of Neuro-macular Leprosy.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, Nos. 1/2, 89–93.

The statement of R. G. COCHRANE that many cases of leprosy never become active has led the writer to record his experience on the evolution of early

neuro-macular cases. Among 55 untreated Ns 1 cases, with few bacilli in the lesions, examined in 1935 and again in 1940, 29 had remained stationary, 4 had improved and 22 were worse, and one of the latter had developed towards the lepromatous type. Further, among 34 early neuromacular tuberculoid cases, Nt 1 of the Cairo nomenclature, 21 showed no change, 6 had improved and the remaining 7 had grown worse ; one of these had developed towards the lepromatous state (L2), in 4 more the skin lesions had increased and in the remaining 2 grave mutilations had occurred. On the other hand, among similar patients treated with oil of Caloncoba and sodium gynocardate rapid improvement took place, which the author regards as being due to specific treatment with favourable results. He agrees with other workers that treatment is least effective in the case of patients in poor general condition, which is often due to helminthic and other complications. *L. Rogers.*

Davey, T. F. **Some Observations on the Role of Allergy in Leprosy (2). Part II. Allergy and the Macular Series.** *Leprosy Review.* 1946, Oct., v. 17, No. 3, 75–87. [10 refs.]

The author considers that the three recognized varieties of macular leprosy, namely, lepromatous, simple neural (flat) macules, and tuberculoid macules, are insufficient for the description of this type of lesions. He considers that a larger variety of forms occur shading one into another and varying between the mildest one, namely localized lesions of the mildest tuberculoid form and pale flat macules, up to—at the other end of the scale—innumerable poorly defined macules of the lepromatous group with no effective localization and representing a temporary phase in the advance of the infection. The mild types give positive lepromin reactions and those at the other end of the scale give negative ones. The author thinks that an allergic mechanism underlies all macular forms of leprosy, as they may appear suddenly. A table of lepromin reactions in six groups that are described gives progressively more doubtful or negative reactions as the lepromatous type is approached. In the raised macule series, positive results were 77–90 per cent. *L. Rogers.*

Tisseuil, J. Essai d'interprétation de la réaction de Mitsuda. [**Interpretation of the Mitsuda Reaction.**] *Bull. Acad. Méd.* 1946, v. 130, Nos. 27/28, 499–502. [26 refs.]

This is a brief discussion of the nature of the Mitsuda reaction. The author points out that in cutaneous leprosy the reaction is negative, because all the tissues, even those apparently healthy, contain the lepra bacilli, and it is specific because other acid-fast bacilli, including those of Stefansky, give positive reactions. Moreover, in lepromatous cases the reaction becomes positive in the case of cures with disappearance of the lepra bacilli from the tissues, and it again becomes negative in the case of relapses of the infection. The true nature of the reaction in this class of cases remains to be determined. On the other hand, in tuberculoid leprosy the reaction is positive both in the healthy and in the involved skin, although very few bacilli are present in the thickened patches ; but it is not specific, because reactions are also produced by paratuberculous bacilli, such as those of Kedrowski and of Clegg, as well as by Stefansky's bacillus. In this form, it is therefore difficult to speak of allergy because different bacilli give reactions. In healthy persons reactions are obtained in some cases. *L. Rogers.*

WHARTON, L. H. **Promin Therapy.** *Leprosy Review.* 1946, Oct., v. 17, No. 3, 96–8.

The author reports on the treatment with promin for one year of seven C3 lepromatous cases of leprosy in the British Guiana leprosy hospital, all young adults who were rapidly going downhill under chaulmoogra treatment. They were all complicated with chronic ulcers of the legs, nodules on the hands and face and oedema, and two patients were nearly blind. Two grammes of promin were injected intravenously daily for six-day periods followed by one day's rest, and the dose gradually increased by 1 gramme weekly to a maximum of 5 grammes. After six weeks' treatment one week of rest was allowed. At the end of a month, general improvement was seen; after three months ulcers were healing and oedema subsiding, the eye conditions appeared to be arrested; and in six months chronic ulcers had healed and nodules were flattening. During the second six months, improvement continued, but in seven cases lepra bacilli had decreased in the nodules, but not in the nose. *L. Rogers.*

FAGET, G. H., POGGE, R. C. & JOHANSEN, F. A. **Promizole Treatment of Leprosy. A Preliminary Report.** *Pub. Health Rep.* Wash. 1946, June 28, v. 61, No. 26, 957–60, 4 figs. on 3 pls.

Promizole is the trade name for 2,4′-diamino-5-thiasolyl-phenyl sulphone. It was made as a less toxic compound than promin. It did not give encouraging results in tubercular disease except in skin forms, but was considered worthy of trial in leprosy on account of its relative non-toxicity by the mouth and its close resemblance to diasone. The present preliminary report is published because it appears to produce more rapid clinical progress than the other two mentioned sulphones. Among 11 patients treated for one year, it was given up in two because of toxic reactions, 1 absconded and 1 died of a cerebro-vascular accident. After six months' treatment with doses of 0·5 gm., gradually increased to 2 gm., thrice daily in the course of several weeks, objective clinical improvement was noted in some of the patients, so 8 more were added, making 15 under treatment, until more of the drug is available. Short notes of the seven cases already treated for one year show that they were fairly advanced lepromatous ones; and that definite flattening of nodules (and in some, healing ulcers) have resulted; the former is clearly indicated in the photos. *L. Rogers.*

FAGET, G. H., POGGE, R. C. & JOHANSEN, F. A. **Present Status of Diasone in the Treatment of Leprosy. Brief Clinical Note.** *Pub. Health Rep.* Wash. 1946, June 28, v. 61, No. 26, 960–63, 1 pl.

This is a further report on the diasone treatment at Carville in 104 cases of leprosy during 2½ years. The drug was given orally in adults in daily doses gradually increased from 0·33 gm. to 1 gm. and from 0·17 gm. to 0·5 gm. in children. It is usually well tolerated orally, while promin has to be administered intravenously on account of its toxicity. Among 66 patients treated for 6 months or more, 74·2 per cent. were predominantly lepromatous, 20·4 per cent. were mixed and only 5·4 per cent. were neural. In only 19 per cent. were the lesions minimal. At present, 24 per cent. of the treated patients are now bacteriologically negative; this compares favourably even with promin. Objective improvement in nodules has been observed in 65 per cent. of the patients, 23 per cent. show subjective improvement and none is worse. The treatment was discontinued in 31, or 29·8 per cent., of the total cases; these include 6 absconded, 10 showed increased erythema nodosum or eczema, 5 gastric intolerance, 4 haematuria (not seen since early doses were reduced from 1 to 0·33 gm.), 2 anaemia, 2 iridocyclitis, 1 drug fever and 1 hypertension.

Notes and illustrations (those of diasone and of promizole treatment respectively have been misplaced) show definite subsidence of nodular lesions, and 1 of 4 cases of which brief notes are given, had become bacteriologically negative. The authors' therefore conclude that diasone given orally usually improves cases clinically within six months. *L. Rogers.*

Muir, E. **Diasone in the Treatment of Leprosy.** *Leprosy Review.* 1946, Oct., v. 17, No. 3, 87–95.

This is a paper on the treatment of 12 cases of leprosy in England, 10 of which were in a fairly advanced lepromatous stage; the other two were intermediate ones and strongly positive bacteriologically. The usual dose is one gramme a day as twice that dose produces anaemia. It is administered in capsules, each containing ½ gramme, one of which was given on alternate days three times a week, increased in cases showing no contraindications by one capsule each day until a maximum of six capsules are given on each of three days in a week. If any anaemia occurs with haemoglobin below 75 per cent., iron, with liver or yeast, is also given. After each three weeks of full dosage a week's rest from the drug is given. If a reaction occurs the drug must be stopped until it has completely subsided. Tolerance is soon acquired and the dosage may then be pushed up to twelve grammes a week for three weeks in each month. Short notes are recorded of the 12 cases, with the following results. A noteworthy effect was improvement in the condition of the eyes in four cases in which complete blindness might have been expected to result. In seven cases, prolonged chaulmoogra treatment for years had not prevented deterioration in the condition, but after a few weeks' treatment with diasone all had made steady improvement. The cessation of febrile reactions and new crops of nodules was especially noteworthy, but it is too soon to say what the ultimate results will be, and it cannot yet be said whether the drug can be prepared in large quantities at a cost which would allow of its general use in very large numbers of leprosy patients. *L. Rogers.*

Internat. J. Leprosy. Cleveland, Ohio. 1945, Dec., v. 13, 67–81. **The Problem of Home Isolation of Lepers in the Philippines.** By the Leprosy Advisory Committee of the Director of Health.

As a result of repeated attempts of the Philippine Assembly to modify the compulsory segregation law to permit of more home isolation, the Director of Public Health obtained the opinions of some members of the staff of the Bureau on the subject, which are summarized and discussed in this paper. Under the existing law, only bacteriologically positive patients are isolated, and about 3,000 early and little infective nerve cases are being treated, with very encouraging results, at home or at clinics. The early very rigid segregation has been modified by the paroling of negative cases since 1922; the establishment of regional treatment stations in 1928, which permitted the isolation of patients nearer their homes; and by granting pass privileges to segregated cases since 1928. The difficulties and dangers of home isolation for infective cases, and the failure of such measures in Rumania and in South Africa, for example, are emphasized. The findings of leprosy conferences and commissions are quoted, in the light of which the practicability of home isolation is considered. The conclusion is arrived at that at the present time it would not be either practicable or wise to adopt such a measure in a highly endemic country such as the Philippines. *L. Rogers.*

HELMINTHIASIS.

ZARROW, M. & RIFKIN, H. **Intestinal Parasites diagnosed at an Army General Hospital in the South Pacific.** *Amer. J. Med. Sci.* 1946, Sept., v. 212, No. 3, 289–93. [14 refs.]

Routine stool examinations were carried out on patients admitted to a general hospital in the South Pacific war area. The patients had been on service in this area for up to three years. The results are compared with other parasite surveys in the United States [BURROWS, 1944, and HOPP, 1944, see this *Bulletin*, 1944, v. 41, 408 and 879]; South America, 1945 [ROMEU CANÇADO, 1944, see this *Bulletin*, 1944, v. 41, 53]; and the South Pacific [MARKELL, 1945, and MUMFORD & MOHR, 1944, see this *Bulletin*, 1945, v. 42, 468, and 1944, v. 41, 965].

A zinc-sulphate concentration method was used. The findings of protozoa were based on 4,323 stool examinations on 1,114 patients with an average of 3·8 examinations per patient. *Entamoeba histolytica* was found in 4·9 per cent. of cases: this is a low figure compared with other surveys in the tropics. Other findings were *Entamoeba coli* (25·1 per cent.), *Endolimax nana* (19·4 per cent.), *Iodamoeba bütschlii* (4·1 per cent.), *Giardia* (1·5 per cent.), *Trichomonas hominis* (1·4 per cent.), *Enteromonas hominis* (1·2 per cent.), *Embadomonas intestinalis* and *Isospora hominis* (each 0·35 per cent.), and *Chilomastix mesnili* (0·28 per cent.).

The findings of helminthic infections were based on the examinations of 11,358 stools from 3,415 patients, 3·3 stools per patient. The main findings were hookworm (13·2 per cent.), *Trickuris trichiura* (2·4 per cent.), *Strongyloides* (1·5 per cent.), *Ascaris lumbricoides* (0·67 per cent.), *Enterobius vermicularis* (0·41 per cent.), *Hymenolepis nana* (0·23 per cent.), and tapeworm (0·03 per cent.). The doubtful parasite *Heterodera radicicola* was found on 6 occasions. Only in the case of hookworm was there any material increase in worm infection above that reported in the general populations in the United States from which the subjects were drawn.

In a series of 167 patients with ankylostomiasis, the infection was diagnosed by one stool examination in 76·3 per cent. of cases, by two in 89·6 per cent., by three in 95·1 per cent., by four in 98·1 per cent., by five in 99·3 per cent., and in 100 per cent. by six stool examinations. *L. E. Napier.*

LOPES, D. M. A eosinofilia provocada no diagnóstico da esquistosomose. [**Provocative Eosinophilia in the Diagnosis of Schistosomiasis.**] *Hospital.* Rio de Janeiro. 1946, May, v. 29, No. 5, 807–10.

The following is a translation of the author's summary :—

1. Repeated observation of the eosinophile rate in the blood in cases of schistosomiasis is of definite value in diagnosis and control of treatment.

2. In doubtful cases, repetition of the blood examination after further doses of antimony can produce clear negative or positive results.

3. The use of provocative eosinophilia in conjunction with Fairley's complement fixation test is likely to produce a more marked result in those cases where a certain diagnosis or test of cure is required. *H. J. O'D. Burke-Gaffney.*

GOLDSTEIN, A. C. Dépistage rapide de la bilharzioze en milieu indigène aux colonies par l'intradermo-réaction à *Schistosoma bovis*. [**Rapid Diagnosis of Bilharzia Infections by *S. bovis* Intradermal Reaction.**] *Ann. Parasit. Humaine et Comparée.* 1946, v. 21, Nos. 3/4, 129–37. [14 refs.]

Every year many native travellers arrive from all parts of the French Sudan in Macina, where they are employed on special public works. Since a considerable

number of these immigrants are suffering from schistosome infestations, and the appropriate molluscan hosts have been found in the neighbourhood, the author feared a massive outbreak of schistosome infection there.

Facilities did not allow of mass microscopic examination or treatment: the author, therefore, impressed by the report of KHALIL and HASSAN (this *Bulletin*, 1932, v. 29, 741) on the *S. bovis* skin reaction, prepared an antigen from this species of schistosome, which is very common in local cattle.

The extract was made with 100 male and female *S. bovis*, crushed in 35 cc. of saline and allowed to soak in the shade in a cool place. The extract was filtered 48 hours later.

The extract was injected into the dermis, as the author found the "cuti-reaction" difficult to interpret in very dark skins. One drop of the filtrate was injected beneath the dermis in the deltoid region, and an injection of distilled water made a finger's breadth lower down.

A positive test appears early and gives the following reactions:—

1. A rise of temperature to 100°–101°F. two to three hours after injection and rarely later, which disappears rapidly in about two hours more.

2. Induration and infiltration of the skin at the site of injection, attaining the size of a small pea. This follows shortly after the rise of temperature and disappears soon after it.

3. Local pain and heat at the site of the infiltration.

In the author's opinion, the induration is the only sign of value, and it is easily seen and palpated.

He obtained positive results in all of 9 persons suffering from schistosomiasis; completely negative results in four others suffering from ankylostomiasis and flagellate infestation; and negative results in 46 healthy control subjects.

He considers that this skin reaction is of considerable value in areas where schistosomiasis is endemic, and other diagnostic facilities are not readily available, owing to its simplicity and rapidity.

The number of cases recorded does not appear to be sufficiently large to justify a final claim of superiority for this method over other recognized tests; but its simplicity for use in remote areas merits further investigation.

H. J. O'D. Burke-Gaffney.

HALAWANI, A. & HAFIZ, A. **Treatment of Urinary Schistosomiasis Haematobium with a Modified Form of Intensive Treatment using Repodral (Fouadin) Solutions prepared locally from the Powder.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 238–42.

"1. A method is described for the preparation of repodral solution immediately before use. This consists of dissolving 6·5 gms. of the powder in 100 cc., filtering through a fresh piece of high quality filter paper and sterilised by heating to boiling for 15 minutes. This solution should be used the same day only.

"2. One hundred and three patients completed the treatment in the out-patient [department] receiving each ten injections. Twenty-four of these received two more injections each. Eighty-seven cases became apparently cured, *i.e.*, approximately 84·5 per cent.

"3. Toxic symptoms were generally mild, such as rheumatic pains, herpes labialis, occasionally nausea and rarely vomiting, anorexia and insomnia. Rise of temperature occurred in three patients. Urticarial wheals appeared at the site of injections in one patient. The most severe toxic symptom encountered was dysiderosis which affected all four limbs in two patients. This skin manifestation disappeared completely after cessation of treatment."

NAVAL MEDICAL RESEARCH INSTITUTE. Bethesda, Maryland. 1946, Apr. 16, Report No. 7. **Effect of Light and Temperature on Shedding of** *Schistosoma mansoni* **Cercariae** [KUNTZ, R. E.]. 16 pp. [12 refs.]

Kuntz reports the results of experiments on the effect of light and temperature on the shedding of *S. mansoni* cercariae by *Australorbis glabratus*.

The infected snails which were used in the experiments were first kept for three days under "maintained conditions" of light and temperature which consisted of six combinations of the variable factors: (*a*) Light of ordinary laboratory conditions with room temperature of 24–27°C.; (*b*) Light of ordinary laboratory conditions with temperature 21–23°C.; (*c*) In darkness at 24–27°C.; (*d*) In darkness at 21–23°C.; (*e*) In continuous light (24 hours daily) of ordinary laboratory conditions at 24–27°C.; (*f*) In light as in (*e*) at 21–23°C.

The snails were removed from the "maintained conditions" to altered conditions which consisted of different combinations of bright light, ordinary light and darkness, with temperatures of 17–19°C., 21–23°C., 24–27°C., and 35–37°C. Cercariae were counted at intervals of 15, 30 and 60 minutes after the altered conditions were initiated.

It was found that both light and temperature changes definitely affect the shedding of cercariae, but that abrupt changes in temperature exert more influence on the shedding than abrupt changes in light intensity. It was possible to force the snails to shed cercariae either three times during the same day or in moderate quantities daily for a period of 5 to 9 days by means of bright light and elevated temperatures. (Normally the snails liberate cercariae only once daily, in a single period from 10 a.m. to 2 p.m.)

No deleterious effects on the snails or cercariae were observed as a result of this forced shedding. *J. J. C. Buckley.*

HERNANDEZ MORALES, F. & MALDONADO, J. F., in collaboration with C. K. PRATT. Diagnostico de la esquistosomiasis de Manson por medio de la biopsia del recto. [**Diagnoses of** *S. mansoni* **Infections by means of Rectal Biopsy.**] *Bol. Asoc. Med. de Puerto Rico.* 1946, July, v. 38, No. 7, 253–63, 5 figs.

—— & —— with ——. **The Diagnosis of Schistosomiasis Mansoni by a Rectal Biopsy Technique.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 811–20, 5 figs.

The authors obtained very satisfactory results with six months' trial of a modification of OTTOLINA and ATENCIO's biopsy of the rectal mucosa in the diagnosis of *S. mansoni* infections.

The results were compared with concentration methods of stools, and antigenic skin reactions, both in treated and untreated cases.

The biopsy method revealed in the aggregate the presence of ova in 100 per cent. of cases, whilst concentration tests produced only 40 per cent. of positive results; only 62 per cent. were found positive amongst 16 patients upon whom the intradermal test was performed.

Positive biopsy results were also found in 70 per cent. of treated cases: concentration methods were only effective in 18 per cent. of these, and the intradermal test was very variable in this group. *H. J. O'D. Burke-Gaffney.*

VOGEL, H. Ueber die Nachkommenschaft aus Kreuzpaarungen zwischen *Bilharzia mansoni* und *B. japonica*. [**Cross-Breeding of** *Schistosoma mansoni* **and** *S. japonicum*.] *Zent. f. Bakt.* I. Abt. Orig. 1942, Oct. 28, v. 149, No. 5, 319–33, 1 fig.

The author in 1941 published the results of pairing female schistosomes with males of another species and showed that they develop normally, copulate and

produce ova, but always of the type of the female worm. Whether further development of such ova would take place was considered a question worth following up and experiments were undertaken to infest some suitable snail intermediate host.

Of the various combinations of the three common schistosomes, *haematobium*, *mansoni* and *japonicum*, two only resulted in enough ova being obtained for further experiment, *viz.* male *mansoni* and female *japonicum* and *vice versa*. Eight mice and two hamsters were used for the crossing of male *japonicum* and female *mansoni*, and five mice and two hamsters for the opposite. The results in each of the experimental animals are detailed ; they may be summed up as follows : Many, in fact the majority, of those produced do not develop at all, but die in the tissues of the host ; a few go on to produce embryos, but usually these soon die and disintegrate ; very occasionally the ovum proceeded to the miracidium stage. Those resulting from pairing male *mansoni* and female *japonicum* could infect *Oncomelania hupensis* or the two ordinary *mansoni* hosts, *Planorbis guadalupensis* and *P. pfeifferi*, but those resulting from the union of male *japonicum* and female *mansoni* went on to the cercarial stage in *P. pfeifferi* only, and even in it infection was rare and the cercariae themselves were, in form and behaviour, like the normal *mansoni* (*i.e.* the maternal species) and the adult worms from these had the characters of *S. mansoni*. Since the final product always " took after " the mother, the ova may have developed parthenogenetically, or the spermatozoa may have acted merely as a stimulus to development, without taking any part in the actual development (pseudogamy).

H. Harold Scott.

HALAWANI, A. **The Effect of Gammexane on the Snails " Planorbis " and " Bulinus ", the Intermediate Hosts of Schistosomiasis in Egypt.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 197–206.

" 1. It was found that in the laboratory and field experiments Gammexane in powder form is destructive to the snails (Bulinus and Planorbis) in a dilution of approximately 5–6 parts per million after 24 hours.

" 2. It is believed that much lower dilutions are sufficient for eradication if applied for a longer time."

KUO, S. C. **Further Studies on Distribution of Schistosomiasis Japonica in Szechwan Province, China.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 367–8.

" 1. Cases of schistosomiasis japonica are now known from eleven districts in Szechwan, a province formerly thought to have few cases of schistosomiasis.

" 2. The presence of *Schistosoma japonicum* in the mesenteries of cattle coming from different districts indicates a wider range of distribution.

" 3. A new subspecies of snail has been found to be capable of acting as intermediate host for *S. japonicum*.

" 4. In addition to *S. japonicum*, *Ornithobilharzia turkestanicum* is common in the mesenteries of cattle of Szechwan."

FAUST, E. C. & INGALLS, J. W., with the assistance of J. K. SEE. **The Diagnosis of Schistosomiasis Japonica. III. Technics for the Recovery of the Eggs of *Schistosoma japonicum*.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 559–84. [11 refs.]

In light human infestations with *S. japonica*, whether primarily so or as a result of partially successful previous treatment, eggs of the worms may be so

scanty in the stools that they cannot be found by examination of simple coverslip preparations of faecal material. A concentration technique must therefore be used for their recovery. With raw material obtained from naturally infected human cases and from experimentally-infected dogs, the authors re-examined the recognized methods of concentration of the eggs, and tried various modifications in an endeavour to develop a technique yielding consistently satisfactory results. They record the details of their extensive experimental work in considerable detail, and show how they improved their technique, step by step, as each modification was introduced after thorough testing. They end with the following conclusions and summary :—

" (1) *Direct fecal films.* These should always first be made and examined in all cases suspected of having schistosomiasis japonica. Three to eight such films provide considerable evidence of the presence of *Schistosoma japonicum* eggs in the stool and are particularly useful in indicating the unequal distribution of the eggs in a stool specimen. Moreover, direct fecal films are especially valuable for the examination of flecks of mucus, with or without blood, in which nests of eggs may be trapped.

" (2) *Sedimentation.* This technic is a simple diagnostic procedure whereby an appreciable amount of faeces may be processed so that a relatively high concentration of *S. japonicum* eggs may be effected. For efficiency the specimen should be thoroughly homogenized manually, or preferably in an electric mixer. It should then be thoroughly suspended in at least twenty-five times as much 0·5 per cent. glycerin in tapwater, then poured through gauze (or wire screening) to exclude macroscopic fecal debris. Four layers of Curity surgical gauze have been found to be very satisfactory for this purpose and serve to strain out only a very small percentage of the total number of *S. japonicum* eggs in the specimen. A wetting agent aids the settling of the eggs. Dilute solutions of potassium hydroxide, iron alum, sodium sulphate and detergents all expedite sedimentation but they increase the bulk of the sediment and to that degree dilute the number of eggs per given volume of sediment. On the other hand, 0·5 per cent. glycerin in tapwater does not swell the sediment and provides a yield of *S. japonicum* eggs in a completely natural state and in the same proportion as they occur in the unprocessed stool. Two and one-half to three hours after initiating sedimentation, following three suspensions and decantations, the final sediment may be sampled, with the assurance that a very high proportion of all the eggs will be concentrated in a small volume of sediment. Moreover, three one-tenth milliliter samplings taken from the sediment will deliver a high proportion (20 to 67 per cent.) of all the eggs in the original unprocessed stool specimen.

" (3) *Zinc sulphate centrifugal floatation.* This technic is not satisfactory for recovery and diagnosis of *S. japonicum* eggs, since only a small percentage of the eggs float. Whether they float or remain in the sediment, they are shrunken and frequently constitute a diagnostic risk.

" (4) *Ether centrifugalization.* The tests may be conducted with either an International clinical laboratory centrifuge or an angle centrifuge, each carrying two or four 15 ml. tubes, which should be graduated. A weighed one-gram sample of stool, or if liquid one ml. sample, should be thoroughly homogenized in 5 ml. of the aqueous reagent to be employed and poured through two layers of Curity surgical gauze into the graduated centrifuge tube. An equal volume of ether should be added, the mixture manually shaken up and then centrifugalized at 1,500 rpm for 2 minutes. The tube is removed from the centrifuge, the interphase film between the ether and the aqueous reagent carefully stirred with an applicator to permit settling of eggs caught in this layer, the contents allowed to settle for a minute and the entire supernatant

liquid decanted. The small amount of sediment is then transferred to one or more microscopic slides as required and examined for eggs.

" Fifteen per cent. hydrochloric acid-ether provides a sediment which usually although not invariably gives a higher egg yield than several direct fecal films. The mechanical interaction between the HCl and ether during centrifugalization destroys or distorts all immature and degenerate eggs, and at times some of the mature viable ones. The addition of certain detergents, particularly Triton NE (0·06 ml. per 5 ml. of HCl), increases the yield of eggs because it partially prevents their destruction. Hydrochloric acid (15 per cent.) — sodium sulphate (sp. gr. 1·08) half and half + Triton is distinctly better than hydrochloric acid + Triton, both in egg yield and in diagnostic quality. Sodium sulphate — Triton (without hydrochloric acid) is usually superior, because it provides all stages of the eggs in the sediment in the same proportion as in the unprocessed stool and with excellent preservation. When other reagents, as KOH, $ZnSO_4$, CHOH and the detergent Tween-80, are added to HCl or substituted for HCl, they may at times produce excellent concentration and fair to good diagnostic quality of eggs in the sediment, but they are not as consistently reliable as is $HCl+Na_2SO_4$+Triton or Na_2SO_4+Triton.

" (5) For recovery of the largest number of *S. japonicum* eggs in a small amount (one gram) of stool, the Na_2SO_4 + Triton-ether centrifugalization technic is the best one which has been developed. However, for routine stool examination, sedimentation utilizing 0·5 per cent. glycerin in water is recommended, because the larger amount of stool processed, together with the high concentration of *S. japonicum* eggs in the first three 0·1 milliliter samplings withdrawn from the sediment, give somewhat greater assurance that, if eggs are present in the unprocessed stool, at least some will be recovered from this amount of the sediment. Both the Na_2SO_4+Triton NE-ether centrifugalization technic and sedimentation may be depended on to provide eggs of high diagnostic quality, including immature, mature, degenerate and calcified ones."

[This paper should be consulted in the original by those working on the subject.] *A. R. D. Adams.*

Baroody, B. J. & Most, H. **The relative Efficiency of Water Centrifugal Sedimentation and other Methods of Stool Examination for Diagnosis of Schistosomiasis Japonica.** *J. Lab. & Clin. Med.* 1946, July, v. 31, No. 7, 815–23.

The authors present a modified water centrifugal sedimentation method of faeces examination which was found to be more efficient in detecting eggs of *S. japonicum* than other routine or special methods currently employed.

Ten to 15 grammes of faeces are shaken up for one to two minutes in a 125 cc. Erlenmeyer flask containing about 100 cc. of lukewarm tap water. The emulsion is strained through two layers of wet gauze into a 50 cc. centrifuge tube with a teated bottom, $4\frac{3}{4}$ in. long by 1 in. diameter, and spun for 30 seconds at 1,500 r.p.m. The supernatant fluid is decanted and tap water at 40°C. is added to the tube which is shaken up and spun again. This is repeated about 3 times or until the supernatant fluid is clear. Four drops of the sediment are then examined on a slide under a large cover slip, 22×40 mm. Two slides at least are examined. The total time required for the procedure is 20 to 25 minutes. If no eggs are detected, 10 drops of water are added to the remaining sediment which is left overnight in a warm place and examined next day for miracidia.

The method recommends itself in that it is simple, rapid, requires no chemical reagents and only a minimum amount of standard laboratory equipment. It was found to be more efficient than direct smear examination of stools which were free of easily visible bloody mucus ; or than examination by the acid-

ether, zinc sulphate or brine floatation methods. It is particularly useful for the detection of light asymptomatic infections and for the evaluation of the results of specific therapy. *J. J. C. Buckley.*

MARTIN, W. B., GRAZIANI, J. G., COLLINS, J. & LINCICUM, D. R. **Chronic Infestation with Intestinal Parasites in an Engineer Battalion with particular reference to** *Schistosoma japonicum. Southern Med. J.* 1946, Nov., v. 39, No. 11, 885–8.

In 206 soldiers of an engineering battalion who had been removed from the site of exposure for four months, 19 cases of infection with *Schistosoma japonicum* were discovered. Exposure to infection had occurred over a period of five months during the autumn and winter 1944–1945. Seventy-seven per cent. were found to be infected with one or more pathogenic parasites, only 5 per cent. were found to be free from any intestinal parasite. A past history of prolonged fever with urticaria, weakness, diarrhoea and other abdominal symptoms was the most significant finding in cases of schistosomiasis. The presence of eosinophilia was only suggestive, but no constant or significant changes were noted in the haemoglobin level, erythrocyte count, leucocyte count, the sedimentation rate, or plasma level.

Up to the present, no serious departure from the normal in the cases of schistosomiasis has been revealed, except for the possible significance of a high percentage of palpable livers ; so that the exact significance of the infection in relation to the future health of the patient can be ascertained solely by a prolonged follow-up. *P. Manson-Bahr.*

GELLHORN, A., TUPIKOVA, Natalia A. & VAN DYKE, H. B. **The Tissue-Distribution and Excretion of Four Organic Antimonials after Single or Repeated Administration to Normal Hamsters.** *J. Pharm. & Exper. Therap.* 1946, June, v. 87, No. 2, 169–80, 2 figs. [13 refs.]

This investigation deals with distribution and excretion in hamsters (*Cricetulus* [? *Cricetus*] *auratus*) of two tervalent (tartar emetic and Anthiomaline) and two quinquevalent antimonials (Stibanose and Neostibosan), twenty-four hours after a single injection, after multiple injections and in chronic toxicity experiments. In the first experiment, groups of five animals were chosen at random and after intraperitoneal injection of the four drugs in amounts corresponding to 10 and 20 per cent. of the LD_{50} doses, determined in mice, they were kept in individual cages with an adequate supply of water but received no food. The drug was diluted in saline so that 1 ml. was given per 100 gm. body weight. On killing the animals the organs were collected, gut contents being added to the faeces, and duplicate analyses were made of the antimony content by the rhodamine-B method which has been evaluated by GELLHORN *et al.* in the article preceding that now under review. It consists in digestion by strong H_2SO_4 and HNO_3 to destroy organic matter and a coloured complex is formed by the metal and dye in presence of excess chloride ion. The complex is then extracted with benzol and the optical density of the solution measured in a spectrophotometer at a selected wave-length and the amount of antimony present determined by comparison with a standard calibration curve prepared in the same way. In agreement with other workers it was found that much larger doses of pentavalent than of tervalent antimony compounds were tolerated. The greatest concentration of Sb was found in all cases in the liver and relative to the amounts of antimony injected was greater in the case of tervalent compounds, but valency was not the only determining factor. Only traces of Sb were found in the spleen after injection of tervalent compounds, but with

pentavalent compounds the content was high. In both organs the Sb content was greater after Neostibosan than after Stibanose, although the amount of Sb injected in the case of the former was smaller. In other tissues only traces of Sb were found. The greater portion of pentavalent antimony was eliminated by the kidneys, and by the bowel—probably owing to secretion in the bile—in the case of the tervalent compounds. About 15 to 20 per cent. of the amount administered remained unaccounted for. Determinations similar to the above were made in the case of tartar emetic and Stibanose following daily injections of the same dose for seven days, the animals being sacrificed 24 hours after the last injection. Greater absolute values were found for antimony in the liver in this case, but relative to dosage there was no percentage increase. The results in the two series of experiments were otherwise comparable. The tissue content of Sb following daily injection of the four drugs, until death resulted, again showed that in spite of wide variations in Sb content, the liver was the chief site of localization and that there was relatively little present in other essential organs. An explanation of the greater toxicity of tervalent compounds was not forthcoming. *J. D. Fulton.*

Donaldson, A. W. & Otto, G. F. **Effects of Protein-Deficient Diets on Immunity to a Nematode** (*Nippostrongylus muris*) **Infection.** *Amer. J. Hyg.* 1946, Nov., v. 44, No. 3, 384–400, 3 figs. [33 refs.]

Zimmerman, H. M. **Fatal Hookworm Disease in Infancy and Childhood on Guam.** *Amer. J. Path.* 1946, Nov., v. 22, No. 6, 1081–99, 18 figs. on 4 pls.

An account of 21 cases.

Loughlin, E. H. & Stoll, N. R. **An Efficient Concentration Method (Aex) for detecting Helminthic Ova in Feces (Modification of the Telemann Technic).** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 517–27. [15 refs.]

In most concentration methods, especially Lane's DCF, the majority of the infertile *Ascaris* eggs are lost. The acid-ether-xylol, or AEX technique, obviates this and certain other limitations of the recognized concentration methods. Advantages of the AEX are that a generous sample of stool is taken initially and yet the portion examined is relatively very small, so that the whole of it can be examined and a quantitative result obtained; and that xylol helps to reduce the adhesive properties of the coagulum and thereby saves the loss of many ova.

"The steps in AEX are as follows:

"1. Measure 4 ml. (or grams) of feces into a dilution counting flask which has been filled to the 56 ml. mark with water.

"2. Add several glass beads (6 mm.), and after giving the preparation an initial shaking, set aside for several hours or overnight (preferably refrigerate); complete the comminution of the feces by vigorous shaking, so that all the eggs are free.

"3. Shake to produce a thorough distribution of the eggs in the fecal suspension and transfer immediately 1·5 ml. of the suspension to a 15 ml. pointed centrifuge tube.

"4. Add 3·5 ml. of 20 per cent. hydrochloric acid [20 ml. concentrated acid diluted to 100 ml.], put a rubber stopper in the tube and shake for one minute; allow to stand for two minutes.

"5. Add 5 ml. of a freshly prepared mixture of equal parts ether and xylol and again shake for one minute.

"6. Centrifuge at 1800–2000 RPM for two minutes and allow the centrifuge to come to a stop gradually without interference.

"7. Separate the semi-floating coagulum from the walls of the tube with a thin wooden applicator.

"8. Decant quickly, permitting the sediment in bottom of tube to remain undisturbed. Then, while holding the tube almost horizontally, clean any adhering coagulum from the inside of the tube with an applicator covered with gauze.

"9. Add one drop of 0·1 N solution of sodium hydroxide to the sediment, mix thoroughly with a capillary pipette, transfer entire suspension to a glass slide and place a coverglass on it. If the density or amount of residue warrant it, make two drops of the material and cover each with a coverslip in order to secure a preparation which will allow the eggs to be seen easily. We prefer a $1\frac{1}{2} \times 3$ inch slide and a 22×30 mm. or 25 mm. square coverslip.

"10. Examine the whole preparation for eggs. Those found are from 0·1 gram. of the original fecal specimen."

Practical tests involved two groups; in the first, 100 consecutively-received faecal specimens for general parasitological examination *plus* 34 sent specifically for examination for ova of *Schistosoma japonicum* were examined in the authors' laboratory. The Telemann (40 per cent. hydrochloric acid) and Lane's DCF techniques were used for comparison. Except that fertile *Ascaris* were recovered in 100 per cent. of positive stools by all three methods, the AEX proved superior with all helminth ova. In the case of *S. japonicum*, the AEX revealed ova in 19 specimens, whereas the Telemann revealed them in only one and the DCF in none. The AEX alone revealed infertile *Ascaris* ova in 13 specimens. Of 15 specimens in which the AEX revealed *Trichuris* ova, the Telemann revealed ova in 8 and the DCF in 11.

The second field test was carried out in Okinawa, where 250 consecutive stools of natives were examined. There were 14 hookworm, 10 fertile *Ascaris*, 4 infertile *Ascaris*, and 20 *Trichuris* infections revealed by AEX that were missed by single dilution counts. In stools with egg-counts of 1,100 eggs or more per gramme, all were positive by the AEX method, and in those with under 1,100 eggs per gramme, 100 per cent. of *Trichuris* and fertile *Ascaris* infections, 90 per cent. of hookworm infections and 67 per cent. of infertile *Ascaris* infections were revealed by this method. *L. E. Napier.*

BLACK, T. C. **Coexistent Hookworm and Tuberculosis.** *Southern Med. J.* 1946, Nov., v. 39, No. 11, 881–4. [15 refs.]

Hookworm infection remains a major public health problem in Florida. During six years, stool examinations on 1,170 admissions to the Florida State Tuberculosis Sanatorium were carried out. The hookworm infection rate was 10·45 per cent. for white males and 6·06 per cent. for white females, or 8·48 per cent. for the whole white group; for the negroes it was only 4·44 per cent.

Among 711 patients discharged during the six years, 60 had hookworm infection. Seventy-three and three-tenths per cent. of the hookworm-positive patients discharged were classified as "improved" or "better", compared with 75·7 per cent. amongst the hookworm-free patients. However, if sputum-positive (tubercle bacilli) cases only are considered, the figures are 63·4 per cent. with hookworm and 70·5 per cent. without hookworm.

The hookworm infections were subclinical in most instances, but a few patients were anaemic, and there is a definite difference between those with haemoglobin above and below 80 per cent.; of the former 78·9 per cent. were discharged as "improved" or "better", compared with 59·0 per cent. of the latter.

Only 22 of 84 hookworm-positive white patients had haemoptysis. This does not indicate any effect on the lungs from migratory larvae, nor was there any evidence that they produced shadows on the chest films.

There are thus two slightly unfavourable prognostic trends revealed, namely, hookworm infection in patients with tubercle bacilli in their sputa, and hookworm infection associated with anaemia in tuberculosis. *L. E. Napier.*

WATSON, J. M. **The Differential Diagnosis of Hookworm, Strongyloides and Trichostrongylus with special reference to Mixed Infestations.** *J. Trop. Med. & Hyg.* 1946, Oct.–Nov., v. 49, No. 5, 94–8, 1 fig. [20 refs.]

Diagnosis of hookworm or *Strongyloides* infections by microscopical examination of faeces is not difficult since, normally, eggs only of hookworm and larvae only of *Strongyloides* are encountered. In double infection with these helminths any doubts as to their identity can be resolved by culturing the faeces, when hookworm eggs, if present, will develop to rhabditiform larvae in 48 hours at 25–30°C. and *Strongyloides* larvae will have developed into free-living adults. Rarely, a single *Strongyloides* infection may show both eggs and larvae in the stool. In this event the eggs are invariably embryonated and slightly smaller than hookworm eggs, measuring 50–58×30–34μ. Rhabditiform larvae of doubtful identity in old or constipated stools may be recognized as those of *Strongyloides* by the short buccal capsule and rather stumpy tail and of hookworm by the long buccal capsule and more attenuated tail. The infective larva of *Ancylostoma* differs from that of *Necator* in the length of the buccal spears and the appearance of an intervening space between oesophagus and midgut in *Necator*.

Eggs of *Trichostrongylus* differ from those of hookworm in size and appearance. They are larger than hookworm eggs, are more sharply pointed at one end, have a larger number of blastomeres and in fresh specimens have a greenish tinge. First-stage larvae of *Trichostrongylus* have a dorsal bend at the level of the anus and the tail terminates in a minute knob. *J. J. C. Buckley.*

LOPEZ-CHAVEZ, G. J. Frecuencia, diagnostico y tratamiento del *Strongyloides stercoralis*. [**Frequency, Diagnosis and Treatment of** *Strongyloides stercoralis*.] *Rev. Méd.-Quirurg. de Oriente.* 1946, Sept., v. 7, No. 3, 159–66.

BAZ, I. I. **Distribution of Filariasis in Egypt.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 280–87. [12 refs.]

NEWTON, W. L. & PRATT, I. **Experiments to determine Potential Mosquito Vectors of** *Wuchereria bancrofti* **in the Continental United States. Part 2.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 699–706.

The first part of this work was summarized in this *Bulletin*, 1946, v. 43, 52. The present authors have continued the investigation and have used 9,122 mosquitoes of 16 species; 2,087 of them, belonging to 14 species, took a blood meal during 225 feeding attempts. The results of 1,314 dissections are tabulated and discussed; they show that in susceptible species the infective stage in the development of *Wuchereria bancrofti* was reached usually within two weeks but in *Psorophora discolor* it required 5 to 7 days longer.

Culex restuans and *Orthopodomyia* sp. did not feed. *Anopheles quadrimaculatus, A. maculipennis freeborni* and *Psorophora ciliata* are incapable of transmitting infection as there was no development beyond the first stage. There were only a few dissections of *Psorophora ferox* and *P. howardii* and these were negative. *Aëdes canadensis, Mansonia perturbans* and *Psorophora*

cyanescens are apparently not vectors though studies on these three species are not completed. *Culex salinarius, Anopheles crucians* and *Aëdes thibaulti* could be occasional vectors but their infectibility in these experiments was low. Studies are not yet complete on *Culex erraticus* but it might be a vector to a minor extent. *Culex pipiens* and *Psorophora discolor* are definitely capable of transmitting infection given suitable conditions; the former had a total infectibility rate of 91 per cent. and the latter of 67 per cent. *H. S. Leeson.*

BERCOVITZ, Z. T. & SHWACHMAN, H. **Filarial Survey among Young Puerto Ricans.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, Sept., v. 22, No. 1, 66–81, 1 chart & 2 maps on 3 pls. [Spanish version 82–94.]

A total of 16,439 young Porto Ricans between the ages of 18–38 years were examined for circulating microfilariae by the use of a thick drop of blood collected at night (9.30 p.m.). The amount was approximately 20 cmm. of blood, dehaemoglobinized and stained with Delafield's haematoxylin. A total of 3·42 per cent. were positive for microfilariae of *W. bancrofti.*

With the exception of one reported case of *Mansonella ozzardi* found by HOFFMAN *et al.* [this *Bulletin*, 1932, v. 29, 768] in a patient who had always lived in Vieques, an island lying off the eastern coast, this is the only species of filaria in Porto Rico.

Among 460 individuals who were positive, only 11 gave a clinical history consistent with filarial disease, but there was no correlation between the numbers of circulating microfilariae and the history of symptoms of clinical filariasis. The highest eosinophilia averaged 39 per cent. in a person with hookworm, whipworm and ascaris, and the highest microfilarial count was 396 per 20 cmm. of blood. No correlation was established between the degree of eosinophilia, the number of circulating microfilariae, and the number and types of intestinal parasitic infections. Microfilarial counts in 97 persons varied from 1 to 396 per 20 cmm.; 47·4 per cent. had 15 or less microfilariae per 20 cmm.

The percentage of positive findings were recorded for different age-groups in 8,029 persons. There was a decline from 5·03 per cent. in the 18 to 20-year age-group to 0·92 per cent. in the 36 to 38-year age-group.

[For the geographical distribution and percentage of Porto Ricans with microfilariae for 76 localities in Porto Rico and in the Vieques the original paper must be consulted as being of local interest.] *P. Manson-Bahr.*

BROWN, H. W. & THETFORD, N. D. **Further Studies on the Treatment of Filariasis due to *Wuchereria bancrofti* with Lithium Antimony Thiomalate.** *Amer. J. Hyg.* 1946, Nov., v. 44, No. 3, 379–83.

In 1944 one of the authors reported on the early effects of treatment of filariasis by intramuscular injections of lithium antimony thiomalate [see this *Bulletin*, 1945, v. 42, 53]: they now report on the results of observation of these patients for a period of two years.

The patients were natives of St. Croix, Virgin Islands, an endemic area: they all had microfilariae in their blood at night but no symptoms of filariasis other than glandular enlargement. They were given injections daily in doses of 3 ml. (180 mgm.) for adults and smaller doses for children, for 7 to 28 days. Among 18 patients who were given the French anthiomaline, eleven showed a reduction in microfilariae of 90 per cent. or more, and in four of these the

microfilariae had completely disappeared by the end of the 12th or 24th month; the rest showed an appreciable reduction in microfilariae. Among 17 patients who were treated with the Merck's preparation of this drug, three showed complete clearance of microfilariae.

The authors do not consider that there is any difference in efficacy of the two preparations: the French drug was possibly more toxic, but the samples used were at least five years old, and it is suggested that this might account for the greater toxicity.

None of the patients suffered at any time from severe local reactions as a result of the deaths of the adult worms in their tissues.

A study of plasma-antimony levels did not suggest that there was any difference in the rate of excretion of antimony between those who did and those who did not respond well to treatment. *L. E. Napier.*

PEEL, E. & CHARDOME, M. Sur des filarides de Chimpanzés "Pan paniscus" et "Pan satyrus" au Congo belge. [**Filarial Worms in Chimpanzees, *P. paniscus* and *P. satyrus* in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 117–56, 23 pls. [23 refs.]

This account of the finding of adult filarial worms and microfilariae in chimpanzees is an interesting and important contribution to present knowledge of certain filarial infections in man.

Microfilaria streptocerca, first found by MACFIE and CORSON in 1922 in the skin of Gold Coast natives, is here recorded from the skin of six out of 11 chimpanzees (*Pan paniscus* and *P. satyrus*) in Belgian Congo. Prolonged search for the parent worms yielded two adult females and a fragment of another, in the connective tissue of the skin of *P. paniscus*. These are described in detail and assigned to the genus *Dipetalonema* Diesing, 1861. The relationship between the parent worms and the microfilariae is established by a comparative study of microfilariae from three sources, the uteri of the adult worms and human and anthropoid skin.

Dipetalonema vanhoofi n. sp. was discovered in fibrous nodules situated in the aponeuroses of the gall bladder and in the investing membranes of the *vena descendens* of chimpanzees. The nodules usually contained a female and two males and were surrounded by a fibrous exudate. Previously the authors had found a single adult female between the mesenteric folds and a fragment of a male on the pancreas. The new species resembles *D. perstans* closely but differs from it chiefly in its smaller size, the greater distance of the genital pore from the anterior end in the female, the smaller spicules and the greater number of adanal papillae (seven pairs) in the male. *Mf. vanhoofi* occurred in the blood and resembles *Mf. perstans* closely. The authors believe that previous records of *Mf. perstans* in the blood of anthropoids are in reality referable to *Mf. vanhoofi*.

In addition to *Mf. streptocerca*, two other species were found in the skin of chimpanzees, *Mf. rodhaini*, n. sp., and *Mf. binucleata*, n. sp.

Mf. rodhaini is characterized mainly by its great length and small width, which average 329·8μ and 2·48μ (maximum mean) respectively. In some specimens, instead of a single excretory cell, there are three special cells posterior to the excretory pore. A fragment of an adult female worm having a sharply pointed tail, was also found in the skin. As this was not referable to *D. perstans* or *D. streptocerca*, it is suggested it may be the parent form of *Mf. rodhaini*.

Mf. binucleata, like the previous species, is sheathless and is characterized by the fact that the anterior and posterior parts are about the same width and by a double body nucleus near the tip of the tail. *J. J. C. Buckley.*

RODHAIN, J. Corollaire à l'étude de E. PEEL et M. CHARDOME sur les filaridés des chimpanzés au Congo belge. [**Note on Peel and Chardome's Work on Filarial Worms in Chimpanzees in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 157–60.

In the light of the recent discoveries of PEEL and CHARDOME (see previous abstract), Rodhain admits that his former opinion that *Paraloa anthropopitheci* Rodhain and van den Berghe, 1939, is the parent form of the *Mf. perstans* (*sic*) recorded in African anthropoids, is no longer tenable. *J. J. C. Buckley.*

DEFICIENCY DISEASES.

O'DONNELL, J. E. **Painful-Feet Syndrome.** [Correspondence.] *Brit. Med. J.* 1946, Nov. 9, 709.

The author, a Major in the I.M.S., refers to PAGE's article [this *Bulletin*, 1946, v. 43, 1060]. When the Dutch East Indies capitulated in March 1942, some 3,500 Allied prisoners, mostly British, were interned in Tandjoeng Priok, Java. In July, the painful-feet syndrome developed and three months later there were some 1,000 cases in the camp. The clinical features corresponded with those described by Page, except for the absence of gangrene, attributed by the author possibly to the warm climate.

In October, when canteen supplies were permitted in the camp, it was found that about 80 per cent. of the sufferers were relieved completely in a fortnight as a result of a daily ration of 100 gm. of boiled *Kachang idjau* (a small type of green pea).

Later, a crude liver extract was obtained from outside sources for the treatment of " blurred vision". It was of no apparent value in this complaint, but it greatly improved, and sometimes cured, the condition in patients who also suffered from painful feet.

The quantity of this product was limited, but 2 cc. were injected intramuscularly at intervals of 2 or 3 days in a few patients, suffering from persistent painful feet, and rapid recovery followed. [It would be of practical interest to ascertain the botanical nature and biochemical assay of *Kachang idjau*.] *H. J. O'D. Burke-Gaffney.*

MONTEIRO, A. M., COUTINHO, H., JANZ, G. J. & DE LOUREIRO, J. A. **Endemic Pellagra in Northern Portugal.** *J. Hygiene.* 1946, Sept., v. 44, No. 6, 518–25. [33 refs.]

Pellagra is endemic among the peasants of Northern Portugal, whose diet consists mainly of white maize, dried beans, olive oil and cabbage. In a population of about 3,000, 100 pellagrins were seen in the course of a month. Thirty of these were investigated in some detail. In most cases there was a long history extending over two years or more. The chief symptoms were weakness, loss of weight, and abdominal discomfort. The most important objective finding was a symmetrical dermatitis of exposed areas, with erythema, pigmentation, and desquamation. This differed from the classical description of pellagrous dermatitis in that there was no sharp line of demarcation between normal and affected skin. The tongue did not have the typical " raw beef " appearance ; in most cases there was an atrophic glossitis of the tip and edges with fissuring. Diarrhoea was usually absent. Changes in the reflexes were slight and inconstant. Frank psychoses were not found, but most patients were depressed and irritable. There was a tendency for the blood pressure to be raised.

On treatment with nicotinamide (0·5–1·0 g. daily), the dermatitis disappeared; the reflexes, if they had been altered, became normal; and the mental and digestive symptoms were relieved. In some cases there was a fall in blood pressure.

Examination of the blood showed a moderate degree of anaemia, with a tendency to macrocytosis. The concentrations of protein, calcium, phosphorus, carotene, and vitamin A were within normal limits. The nicotinic acid excretion was measured in a number of samples of urine chosen at random, and was found to be low.

The diet was investigated in some detail in 18 families, comprising 86 people, of whom 33 were pellagrins. The average intake per day was: calories 3,000 (70 per cent. from carbohydrate); protein 81 gm. (70 gm. from vegetable sources); nicotinic acid 11·73 mgm. The supply of calcium, phosphorus and iron was adequate. The intake of vitamins A, B_1, B_2 and C was slightly below the optimal requirement.

In discussing their findings, the authors point out that they are dealing with a form of pellagra which is mild, chronic, and pure, since it is not associated with evidence of riboflavin or vitamin B_1 deficiency. The question arises: why should pellagra occur on a diet which is not very low in nicotinic acid? The recognized requirement is 15–20 mgm. a day, and the average intake in the population investigated was nearly 12 mgm. daily. It is suggested that the requirement of nicotinic acid is increased by a shortage of animal protein, and more specifically by a deficiency of individual amino-acids such as tryptophane and lysine. When the diet is adequate in calories and total protein, but deficient in animal protein, maize has a special effect in producing pellagra; on a low calorie and low total protein intake, pellagra may occur on any vegetarian diet.

[The problem of why pellagra is associated with a diet of maize has not been solved by the identification of nicotinic acid as the pellagra-preventive vitamin. Aykroyd and Swaminathan [see this *Bulletin*, 1940, v. 37, 797] showed that the maize diet of Rumania, where pellagra is endemic, contained more nicotinic acid than the poor rice diet of India, where pellagra is uncommon. Therefore attention has again been directed to the old toxic theory on the one hand, and to the possibility of an amino-acid deficiency on the other, since it has long been known that maize protein is deficient in tryptophane and lysine. Recent findings throw new light on these relationships, though they do not explain them. Krehl *et al.* [*Science*, 1945, Mar. 16, 283] showed that the inclusion of maize in a low protein diet for rats caused a retardation of growth, which was prevented by tryptophane or nicotinic acid. Woolley [*J. Biol. Chem.*, 1945, v. 157, 455; *ibid.*, v. 162, 179] found that 3-acetylpyridine, the ketone analogue of nicotinic acid, had a toxic effect on mice, which was prevented by both nicotinamide and by tryptophane. He also succeeded in extracting from maize a substance which produced a pellagra-like syndrome in mice—failure of growth, mild diarrhoea, and reddening of the skin and tongue [Woolley, this *Bulletin*, 1946, v. 43, 1160]. Kodicek *et al.* [this *Bulletin*, 1947, v. 44, 119] suggested that the pellagragenic agent in maize is indole-3-acetic acid, a substance which can be formed by the oxidative deamination of tryptophane. This adds interest to the observation of Watson [*Proc. Soc. Exper. Biol. & Med.*, 1939, v. 41, 591] that the urinary pigment which gives a red colour in the Beckh-Ellinger-Spies test is urorosein, a derivative of indole-acetic acid. This test, however, is not specific to pellagra.

It is clear that we are on the verge of new developments in our knowledge of pellagra. The paper from Portugal is a useful reminder that the last word has not been said with the discovery of nicotinic acid.] *J. C. Waterlow.*

YUDKIN, J. **Riboflavin Deficiency in the West African Soldier.** *J. Trop. Med. & Hyg.* 1946, Oct.–Nov., v. 49, No. 5, 83–7.

In 1945 an investigation was made into the condition of some 1,050 West African troops in Sierra Leone. Signs of riboflavin deficiency—scrotal dermatitis, glossitis, and angular stomatitis—were found to be very common. The incidence, in a number of different units, was about 20 per cent. Treatment with yeast tablets, compound vitamin tablets, or pure riboflavin caused a rapid improvement in scrotal dermatitis in nearly all cases. When 9 mgm. of riboflavin per day were given, healing was complete in 3 to 4 days. The tongue changes responded less quickly and less uniformly.

An analysis is given of the constituents of the West African ration scale. One of the main sources of riboflavin was millet, which is not normally eaten by Africans in Sierra Leone. Questioning showed that millet was very unpopular among the troops, and that not more than one-fifth of the amount supplied was in fact consumed. Therefore, though the ration scale theoretically provided 1·5 mgm. of riboflavin per day, the actual intake was estimated at only 0·8 mgm. The author emphasizes the importance of taking local food habits into account in the planning of ration scales. *J. C. Waterlow.*

CHAUDERON, J. Avitaminoses dans un corps de troupe colonial. [**Avitaminosis in Colonial Troops.**] *Méd. Trop.* Marseilles. 1945, July–Aug.–Sept., v. 5, No. 3, 228–36.

The urinary elimination of bisulphite-binding substances (B.B.S.) was measured in a number of French Colonial and European troops. High values were found, both in apparently normal subjects and in a small number of patients with complaints ranging from a wound which would not heal to "hepatic asthenia". It is considered that the unit as a whole was suffering from vitamin B_1 deficiency, overt or subclinical. The men were subsisting on American Army rations, supplemented by bread and wine, and later by fresh fruit and dairy products. *J. C. Waterlow.*

HAEMATOLOGY.

LEAVIS, Hetty. **Haematological Standards in Southern Rhodesia : a Survey of 100 White School Girls.** *South African Med. J.* 1946, Nov. 23, v. 20, No. 22, 715–18.

DAVIDSON, L. S. P. & GIRDWOOD, R. H. **Folic Acid in the Treatment of Megaloblastic Anaemia.** *Lancet.* 1946, Sept. 14, 373–6.

Six cases of Addisonian pernicious anaemia, with typical megaloblastic bone-marrow and histamine-fast achlorhydria but with no neurological signs and no preceding history of diarrhoea or dietary deficiency, were given folic acid, four of the patients receiving doses ranging from 5 to 20 mgm. by mouth daily for several weeks, the fifth 200 and 100 mgm. intramuscularly at an interval of a fortnight, and the sixth a single dose of 400 mgm. orally. Of those receiving daily oral treatment, only one who received 20 mgm. daily had a satisfactory reticulocyte response and red cell increase, the reticulocytosis in others receiving only 10 or 5 mgm. daily being suboptimal ; the large doses given by mouth or parenterally produced excellent responses, which if obtained regularly might show that the simplest and most effective treatment might be an initial large dose followed at weekly or fortnightly intervals by doses of 50–100 mgm. In all six cases the bone-marrow became transformed from a megaloblastic to a

normoblastic state, and the clinical condition of the patients improved coincidentally with the blood. The observations suggest that the therapeutic daily dose by mouth is between 5 and 20 mgm., and that at present it would be safer not to reduce the daily dose below 20 mgm. in the treatment of pernicious anaemia. The maintenance dose has yet to be settled.

Three cases of refractory megaloblastic anaemia, not responding to parenteral liver therapy but responding to proteolysed liver given by mouth, were also treated with folic acid by mouth in doses up to 20 mgm. daily. In each case, the drug produced a rise in reticulocytes, red cells, and haemoglobin, and transformed the bone-marrow from the megaloblastic to the normoblastic state. In no instance, however, did folic acid alone restore the blood picture to normal, and in two of the cases, proteolysed liver by mouth caused a further rise in red cells subsequent to folic-acid therapy. Since megaloblastic anaemias, refractory to anahaemin, respond to both proteolysed liver and to folic acid it might be thought that folic acid is the active principle in proteolysed liver, but as proteolysed liver produced a further response after folic acid had ceased to be effective, it is suggested that in liver and proteolysed liver there exists some as yet undiscovered anti-anaemic principle additional to the specific anti-anaemic factor in anahaemin, and to folic acid. *F. Murgatroyd.*

Bonnin, H., Dubourg, E. & Moretti, G. F. Acide folique et anémie pernicieuse. [**Folic Acid and Pernicious Anaemia.**] *J. Méd. de Bordeaux.* 1946, Oct., v. 123, Nos. 19/20, 361–6. [20 refs.]

The following is a translation of the authors' summary.

The authors record a case of pernicious anaemia treated successfully with folic acid. Following a detailed study of haemograms and marrow-pictures, the authors present a commentary in which, after discussing the main American investigations relevant to the synthesis of folic acid, they give their reasons for believing that folic acid should be likened to the extrinsic factor. They conclude that pernicious anaemia should be envisaged as a deficiency with a double development, in the first place responsive to cure by yeast or folic acid and "réversible", and later strictly liver-curable and "irréversible", the disease recurring after treatment ceases. *H. J. O'D. Burke-Gaffney.*

Stransky, E. & Regala, A. C. **New Type of Familial Congenital Chronic Hemolytic Anemia.** *Amer. J. Dis. Children.* 1946, May, v. 71, No. 5, 492–505. [Refs. in footnotes.]

Four years ago the authors published a paper on erythroblastic anaemia following splenectomy in cases of chronic familial haemolytic anaemia; they believed that they were dealing with an hitherto undescribed clinical condition. One of the patients was a child belonging to a family of five children of whom four were subsequently found to be affected by a similar anaemia; in contrast to ordinary cases of chronic familial haemolytic anaemia, striking features were the erythroblastosis and the severe degree of illness shown by the children.

They have now observed 10 cases of this new type of haemolytic anaemia among Filipinos, but none among white people. It seems to be an inherited, congenital disease, affecting both sexes, unlike the elliptocytic anaemia of Cooley. Anaemia, jaundice and splenomegaly develop in early infancy. The peripheral blood is characterized by severe anaemia, oligocythaemia, oligochromia, extreme anisocytosis and polychromasia. There is neither spherocytosis nor formation of target cells, and the fragility of the red cells is invariably normal. Erythroblastosis is a conspicuous sign; in the peripheral blood it is constantly observed, although the number of erythroblasts seems to be moderate. The

differential count shows a shift to the left of the neutrophils; myelocytes, sometimes myeloblasts and promyelocytes, are present in the majority of cases. The serum icterus index is slightly increased, between 10 and 20 units, and the bilirubin is around 1·5 to 2 mgm. per 100 cc. Jaundice is present constantly, although the icterus is more prominent during the frequent haemolytic crises. There is an increase in the immature elements of the erythroblasts in the bone marrow suggestive of some defect in the maturation of the red cells, contrasting with the findings in typical cases of haemolytic anaemia in which, although there is an increase of the erythropoietic tissue, the different stages of maturation of the erythroblasts are not impaired; consequently the reticulocyte count may be only slightly increased. Very characteristic of the new type of haemolytic anaemia is the further development of the disease after splenectomy. Extreme erythroblastosis develops immediately and lasts for years; erythroblasts, numbering 50,000 to 200,000 have been constantly counted in the peripheral blood, although the reticulocyte count has not corresponded to this high count of nucleated red cells. Anisocytosis and polychromasia grow worse after splenectomy, and a striking macrocytosis, with extreme anisocytosis, develops. The results of splenectomy suggest, therefore, that in this disease the spleen has an influence on the size and maturation of the red cells in the bone marrow, although no such effect is observed in normal persons subjected to splenectomy.

F. Murgatroyd.

FAWDRY, A. L. **Cooley's Anaemia : Notes on Six Adult Cases.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Aug., v. 40, No. 1, 87–91, 1 chart.

The fatal familial anaemia described by Cooley is the most serious form of a disease of varying severity transmitted as a Mendelian dominant by less severely affected "carriers". Examples of the disease include continuous gradations from a fatal anaemia with gross physical change (splenomegaly, hepatomegaly, cardiac enlargement, universal bone-changes, icterus) and obvious dys-haematopoiesis; through moderately severe and disabling refractory hypochromic anaemias with slight physical changes (palpable spleen, slight thickening of the calvarium) and well-marked morphological anomalies of the erythrocytes, but absence of circulating normoblasts; to the mildest disorder obvious only by laboratory examination in an otherwise healthy individual. Harbouring the trait is of no consequence to the individual, who consequently usually survives with the condition unrecognized to adult age; but the potential repercussions on his offspring are obvious.

The haematological features signalling the "trait" in healthy relatives of the anaemic persons are a degree of anisocytosis and poikilocytosis out of proportion to the intensity of anaemia, the presence of target, oval and stippled cells, and an increased resistance to haemolysis by hypotonic saline solutions. Marrow-smears show an increase in the proportion of normoblasts to other nucleated cells.

While it is not possible to say which character of the erythrocytes is pathognomonic of the trait, the fundamental defect is probably the production of abnormally thin cells with a deficient haemoglobin content. The presence of the disorder is most strikingly shown by plotting the fragility curve.

F. Murgatroyd.

FINDLAY, G. M., ROBERTSON, W. M. & ZACHARIAS, F. J. **The Incidence of Sicklaemia in West Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Aug., v. 40, No. 1, 83–6. [14 refs.]

The incidence of the sickle cell trait among 5,500 Africans, whose blood was examined after 24-hours at room temperature in vaseline-sealed cover-glass

preparations, was found to be 12·4 per cent. Just over half the subjects were from the Gold Coast and French Togo, the remainder coming from Gambia, Sierra Leone and Nigeria, where southern tribes, pagans from the Plateau and Hausas were examined. No significant specific tribal differences were noted, and the sex incidence of the trait was approximately equal, 11·2 per cent. in males and 12·6 per cent. in females; but differences were observed in relation to age suggesting that the expectation of life in sicklers may be less than in normal persons. Among pregnant women the incidence of the trait was 16·9 per cent., while among sterile women it was 21·3 per cent. Observations to determine whether the jaundice seen in negroes suffering from pneumonia could be correlated with the sickle cell trait revealed no statistically significant difference between patients with and those without jaundice. Similarly no correlation was observed between the sickling trait and the presence of tropical ulcers of the leg.

No case of the sickle cell trait was found among 568 British soldiers and airmen, temporarily stationed in West Africa, nor among 188 Syrians.

F. Murgatroyd.

DERMATOLOGY AND FUNGUS DISEASES.

DUFFNER, G. J. **Heat Rash as a Problem in the Naval Service.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 539–41.

This paper records an investigation concerning prickly heat which was made at the U.S. Naval Medical Research Institute. Ten volunteers constituted the "Hot Group"; they worked for seven hours each day in a room maintained at 108°F., dry bulb, and 83°F., wet bulb, and spent the remaining 17 hours in another room maintained at 95°F., dry bulb, and 83°F., wet bulb. The work they performed was walking on a treadmill. A similar group of volunteers—the "Cool Group" worked for seven hours a day in the hot treadmill room, but spent the remaining 17 hours in an environment of 85°F. dry bulb and 71°F. wet bulb. The experiment lasted for 10 days.

All the members of the "Hot Group" developed heat rash, some 39 per cent. of the skin surface of each person being involved. Only one person in the "Cool Group" developed the rash, and only 15 per cent. of the body surface was affected.

In a second experiment, 12 seamen, all 18 years of age, were divided into "Hot" and "Cool" groups. Three rooms were used; for the first eight days the rooms were cool (80°F. dry bulb, and 70°F., wet bulb). On the ninth day, the treadmill room was raised to the same temperature as in the first experiment; in the second room, occupied by the "Hot Group" when not working, the temperature was maintained at 90°F., dry bulb, and 85°F., wet bulb; in the third room, which the "Cool Group" used, the original temperature was maintained. The "Hot Group" worked the treadmill for three hours daily. The "Cool Group" worked the treadmill for a similar period, spent nine hours daily in the hot quarters, and then retired to the coolest room for 12 hours. The experiment continued for 30 days. All but one person in the "Hot Group" developed heat rash.

In further experiments, persons were exposed continuously to a temperature of 97·8° dry bulb and 86° wet bulb; the eruption developed suddenly on the third day of the experiment.

The investigators conclude that if a person spends 12 hours a day in an atmosphere "in which one does not sweat at rest" miliaria will not develop.

They found no correlation between the *p*H of the sweat, sweating rates or complexion and the incidence or severity of the rash. Exposure to ultra-violet rays ameliorated the symptoms in some cases, but in others increased their severity.

The histo-pathology of the affected skin was as follows:—hyperplastic epidermis ; vesicle formation in the *stratum lucidum* not related to the sweat glands or hair follicles ; and oedema of the corium. The dermis " gave every indication of a dermatitis " and some of the inflammatory cells infiltrated the epidermis.

R. M. B. MacKenna.

Simons, R. D. G. P. Dermatoses in tropen-krijgsgevangenschap. [**Dermatoses in Tropical Prisoners Camps.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1946, Apr. 20, v. 90, No. 16, 351–5.

Prisoner-of-war camps under the Japanese in Java and Sumatra were as notorious as those elsewhere in the Far East for their overcrowding, insanitation, underfeeding and maltreatment. The author was the head of the Rapwi military hospital and Red Cross Clinic, Batavia. He treats his subject, after an indication of the dietary on which his patients had to subsist from April 1942 to September 1945, under specific heads :—

(1) *Artificial dermatoses.* These were artefacts produced by the guards of the prisoners : haematomas due to blows on the legs or face with loss of teeth and stomatitis ; forced holding of red pepper pods for an hour in the mouth and multiple burns from putting out cigarette ends. (2) *Yaws,* was not seen, nor were those dermatoses which are regarded as often being related causally to nervous shock, namely alopecia areata and lichen ruber. (3) *Scabies.* The chief sites were the wrist, the elbow and the penis, but not so often between the fingers. Failure to recognize scabies accounted for many of the diagnoses of pruritus due to vitamin or calcium deficiency. Pruritus, in fact connoted scabies or pediculosis. (4) *Pyodermia* as might be expected, in the form of furunculosis, etc., was common. (5) *Tropical ulcer.* The phagedenic ulcer rarely occurred in the camp at Bandoeng, but was common in Sumatra where invalids and shoeless persons had to work and wash in contaminated water. Treatment was by pure phenol or iodoform. (6) *Ringworm.* Epidermophyton infection of the foot ("athletic foot") and other tinea infections were a frequent occurrence. Sycosis barbae is a rare condition in the Netherlands Indies and was not seen among the prisoners of war. (7) *Erysipeloid erythema.* Under this name is described a painful, acute, fleeting epidemic condition beginning on the shin or instep, of some 2 to 6 weeks' duration, with slight fever. It may belong to the group, erythema multiforme. (8) *Pellagra,* in all its varied forms was moderately frequent. The author holds definite views on this variability and considers pellagra to be a poly-, if not an omni-deficiency, by no means restricted to B-complex avitaminosis. The pellagra syndrome varies according to the particular deficiency involved and one should not rely rigidly on the old-fashioned triad, dermatosis, diarrhoea and depression (ultimately dementia). The depression may be incidental and dementia patients may also suffer from pellagra. It is suggested that we may be dealing with a vicious cycle : underfeeding—pellagra—intestinal lesions—anorexia—underfeeding. Skin lesions are represented by widespread erythema and sensitivity to sunlight, pigmentation and hyperkeratosis. Thrombocytopenic purpura is a noteworthy feature and is independent of sunlight erythema : it can occur " along the whole course of the alimentary tract" [*Brit. Med. J.,* 1946, Nov. 30, 817]. (9) Other dermatoses dealt with are psoriasis, which became mild because of the diet ; and a few cases of herpes zoster, leprosy and what is called the short-lived skin hobby of tattooing, in which the word " mother " was the most popular pattern.

W. F. Harvey.

MIESCHER, G. Penicillin in der Dermatologie. [**Penicillin : its Use in Dermatology.**] *Praxis.* Berne. 1946, Dec. 23, v. 35, Nos. 51/52, 869–75. [22 refs.]

Owing to the sudden rise in the popularity of penicillin and the varying reports on its success or failure, the time has come, says the author, to take stock of its value in diseases of the skin. If we bear in mind the variable susceptibility to the drug of different strains of the same species of organism, Staphylococcus for example, we shall find a solution, in part at least, for what is otherwise puzzling—that some staphylococcal and streptococcal cutaneous affections react well to it, while others are quite unresponsive.

In *furunculosis* and in *carbuncle* the results have been disappointing ; in a few cases there seemed to be some benefit, but it was not great and was not sustained. In *sycosis* again the results were variable. Of 7 cases referred to, two were cured by a three-day course, another relapsed within 3 weeks, but was healed by a second course, four showed improvement but were not cured. The dose given was 100,000 Oxford units on each of two successive days. In cases of *sudaminal abscess* 100,000 units daily were given. Of nine such, in 3 the collections softened and broke down, in 4 resolution took place without softening or breaking down, 2 were completely unaffected. Seven *impetigo* patients were treated with penicillin ; 4 were cured, but one of these relapsed after 20 days, 3 improved but were not cured until other forms of treatment were substituted. Unexpectedly rapid success followed its use in patients with *staphylococcal follicular dermatitis* ; a local spray was used and also intramuscular injections of 100,000 units for adults and 50,000 for children, for 1–3 days. In *impetiginous eczema* again the results varied ; healing might result from large doses and prolonged use, up to one million units. Lower dosage, up to 400,000 units brought about improvement. In most cases the eczema, on which the pyodermic state had been, as it were, grafted, remained. Penicillin was tried in cases of *ulcer of the leg*, usually of vascular origin. Most of these were unaffected ; some showed a little amelioration at the start, but this was not maintained and, generally speaking, the benefit was negligible. As regards *eczema*, in view of the many possible causes, bacteria, allergy, etc., uniform results could hardly be expected. The inflammation and irritation might subside and staphylococci diminish, but only a few cases were healed by the penicillin. It proved best in *impetigo* and " weeping " eczemas, because in these the staphylococci are a main complicating factor.

To sum up : In staphylococcal affections of the skin, penicillin is a valuable addition to the medical armamentarium. In streptococcal infections it is better to combine the penicillin with one or other of the sulphonamide drugs.

H. Harold Scott.

SEWELL, S. A. **Insulin Therapy in Acne Vulgaris in Tropics.** *J. Roy. Nav. Med. Serv.* 1946, July, v. 32, No. 3, 185–6.

Acne vulgaris in the adolescent male can be very troublesome under service conditions, especially in the tropics. In 1940, the author treated six cases of indurated acne by the injection of 10 units of insulin every morning and afternoon (6 a.m. and 4 p.m.) ; the usual local measures were used concurrently ; one case did not improve ; in the remainder " the inflammatory reaction disappeared " and no further lesions appeared during the next four months.

In 1942 a further series of eight cases were similarly treated with satisfactory results ; residual comedoes were expressed and then 2 per cent. sulphur and salicylic acid ointment was applied. One of these patients is known to have required further treatment two years later.

In 1943, five men suffering from acne vulgaris were treated by the insulin regimen in a temperate climate. Three of these were old-standing chronic cases of considerable severity and did not benefit from the treatment ; in two cases their inflammatory lesions subsided but comedo formation persisted.

In 1944 and 1945 fourteen men were treated with insulin on board ship in the tropics. Concurrent local therapy was not given, except that pus was drained from some indolent lesions. In 12 cases improvement occurred rapidly ; in 2 cases, in which there was much scarring and cyst formation, there was slight, if any, improvement. When insulin therapy ceased, local treatment was commenced. The cases did well and after six months' observation, only two had had a further exacerbation, which responded within three weeks to insulin therapy.

The author does not advocate treatment with insulin as being a cure for acne vulgaris and states that it does not replace local therapy ; but he recommends the drug as being a useful adjuvant which often ensures a remission of the infective phase of the disease. The dosage of insulin which he advocates (10 units twice daily) was chosen empirically ; symptoms of mild degrees of hypoglycaemia were noted only in a few instances and were easily relieved by small doses of cane sugar. *R. M. B. MacKenna.*

JOLLY, A. T. H. **The Effect of intravenously administered Antimony Compounds on Pyogenic Skin Lesions.** *Med. J. Australia.* 1946, Nov. 2, v. 2, No. 18, 630–34.

" 1. Thirty-five cases of suppurative skin lesions and one of an oral lesion treated by the intravenous administration of antimony preparations are cited.
" 2. The follicular type of lesion appears to respond to antimony therapy.
" 3. Antimony is known to have an affinity for keratin.
" 4. The one mucous membrane lesion cited failed to respond to antimony.
" 5. The commonest organism found in the lesions was the staphylococcus."

BERESTON, E. S. & CHENEY, G. **Vitamin B Complex in the Treatment of Lichenoid Dermatitis.** *Arch. Dermat. & Syph.* 1946, Oct., v. 54, No. 4, 425–31.

" 1. The time of recovery from lichenoid dermatitis is shortened by the administration of vitamin B complex in large doses in addition to routine dermatologic care. This improvement occurs in patients with moderate and mild eruptions but not in those with severe ones.
" 2. Vitamin B complex deficiency is a factor, probably secondary, in causing lichenoid dermatitis.
" 3. The fraction or fractions of the vitamin B complex group which are responsible for the more rapid recovery are yet to be determined."

POPOV, I. S. [**Questions of Mycology.**] *Trudy Vseukrainskogo Gosudarstvennogo Instituta Venerologii i Dermatologii.* Kharkov. 1934, v. 5, 133 pp., 24 figs. [In Russian.]

This publication deals partly with work in mycology carried out at the Ukrainian Institute of Venereology and Dermatology between 1931 and 1933, and partly with a review of mycological literature published in the Soviet Union and in other countries, from 1928 to 1933. The work contains the following six articles : (1) " Organization of a campaign against mycoses in the Ukraine " ; (2) " Fungus diseases, based on materials of the Institute for

1931–1933"; (3) "The clinical course, etiology and therapy of dyshidromorphic and intertriginous mycoses"; (4) "The rôle of pathogenic fungi in the etiology of infectious epidermophytoses"; (5) "Mycological and clinical characteristics of dermatomycoses, and their peculiarities"; (6) "Summary of recent achievements in mycology." *C. A. Hoare.*

SHARP, W. B. & JOHN, Mildred B. **Pathogenicity of the Aspergilli of Otomycosis.** *Texas Reports on Biol. & Med.* 1946, v. 4, No. 3, 353–63. [12 refs.]

"1. The fungi associated with otomycosis are of common saprophytic species that abound on the normal skin and in the dust of the air.

"2. The lesion does not harbor indiscriminately all fungi to which the body is exposed, but favors *A. niger*, *A. flavus* and occasional others. We did not learn the nature of the selective factor.

"3. We found little reason to think that a susceptibility of the tissue to attack by these particular fungi was what accounted for their thriving so well in the lesion.

"4. Strains of these fungi which were associated with the disease failed to show properties unshared by other strains of the same species. Otomycosis strains did not form a more toxic group, nor a group distinguishable from other strains of the species by antigenic characteristics."

MESROBEANU, Lydia. Contribution à l'étude de la structure antigénique des "Monilias". [**Study of the Antigenic Structure of "Monilias".**] *Arch. Roumaines Path. Expér. et Microbiol.* 1943, Jan.–Dec., v. 13, Nos. 1/2, 123–32. [12 refs.]

GONÇALVES, A. P. Associação de blastomicose brasileira e tuberculose em lesões ganglionares. [**Association of Brazilian Blastomycosis and Tuberculosis in Lymph Nodes.**] *Rev. Brasileira Med.* Rio de Janeiro. 1946, July, v. 3, No. 7, 525–33, 10 figs. [Summary in English by the author.]

"1. Brazilian blastomycosis and tuberculosis can exist associated in lesions of the lymph nodes. 2. These observations raise to 3 the number of known cases of this association: the first, of Oscar Versiani; and the two others [that it has] just reported. 3. In a patient with a diagnosis of Brazilian blastomycosis, the complementary examination that provides the greatest assurance of detecting the association of the mycosis with tuberculosis in the lymph nodes is the inoculation into guinea pigs. 4. In these cases of lymphadenitic Brazilian blastomycosis where the sulfonamides known as effective in this infection have failed to produce the usual curative results, the possibility of an associated tuberculosis must be suspected and inoculation into guinea pigs should be resorted to. 5. Tubercle bacilli can determine a local ambient unfavorable to the development of *Paracoccidioides brasiliensis*, when they are both present in the same lesions."

BOBLIOLO, L. Granuloma apical (dentário) por "Paracoccidioides brasilienses" (Splendore), Almeida 1929. [**Apical (Dental) Granuloma caused by** *Paracoccidioides brasiliensis*.] *Brasil-Medico.* 1946, Oct. 19 & 26, v. 60, Nos. 42/43, 341–2.

Report of a case.

Niño, F. L. Granuloma paracoccidioidico curado con sulfadiazina. [**Paracoccidioidal Granuloma cured by Sulphadiazine.**] *Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1946, Jan.–July, v. 22, No. 176, 7–27, 9 text figs. & 23 figs. on 6 pls. [23 refs.] [Summary in English by the author.]

"The author makes a clinical and mycological study of a case of Paracoccidioidal Granuloma on a Brasilian man living for 34 years in the City of Buenos Aires. The lesions were situated in mouth, lymph-nodes and the lungs. The patient was treated with Sulphadiazine in large doses and in a long and continued form up to the clinical healing of the lesions. This is the first case of Paracoccidioidal Granuloma treated by Sulphadiazine in Argentina and the patient restored to health."

Mezey, C. M. & Fowler, R. **Cerebrospinal Cryptococcosis.** *J. Amer. Med. Ass.* 1946, Nov. 16, v. 132, No. 11, 632–4.

Bereston, E. S. & Waring, W. S. **Aspergillus Infection of the Nails.** *Arch. Dermat. & Syph.* 1946, Nov., v. 54, No. 5, 552–7, 2 figs.

HEAT STROKE AND ALLIED CONDITIONS.

Kirk, J. B. **Heatstroke and Sunstroke.** *Practitioner.* 1946, Aug., v. 157, No. 938, 107–13.

This paper is a short review of the various syndromes that may result from exposure to heat, with notes on treatment and prophylaxis.

[A number of minor inaccuracies should be mentioned, since they may be misleading in practice.

i. It is stated that all heat-effects have in common, as a causative factor, excessive exposure to radiant energy. In fact, in the stoke-holds of ships, in deep mines, and in the "wet" tropics, there is little or no gain in radiant heat by the body from the environment. This point is of practical importance. When, as in the desert, there is a large radiant heat gain, clothing is of value as a protection against the incoming heat. But when there is no radiation from the environment, it usually happens that the humidity is high. Under these conditions, the most desirable property of clothing is a negative one—that it should not hinder the evaporation of sweat.

ii. It is incorrectly stated that dehydration is present in the condition known as "type II heat exhaustion" [Ladell, Waterlow and Hudson, 1944, this *Bulletin*, 1945, v. 42, 143.]

iii. The clinical phenomena in heat exhaustion are said to be outward manifestations of alterations in the electrolyte balance of the tissue fluids. In so far as it is applied to the syndrome of salt-deficiency dehydration, this statement is unfortunate, since it directs attention away from the real sequence of events and the correct remedial measures. In this condition, the presenting features are those of peripheral circulatory failure, caused by a diminished plasma volume with haemoconcentration; this, in turn, is caused by dehydration, which is secondary to salt-deficiency. In severe cases the immediate treatment of choice is simultaneously to restore the circulation and remedy the salt-deficiency by rapid intravenous infusions of saline.]

J. C. Waterlow.

TROPICAL ULCER.

LIEBOW, A. A., MACLEAN, P. D., BUMSTEAD, J. H. & WELT, L. G. **Tropical Ulcers and Cutaneous Diphtheria.** *Arch. Intern. Med.* 1946, Sept., v. 78, No. 3, 255–95, 18 figs. [Refs. in footnotes.]

During the campaign in the S.W. Pacific, the authors observed large numbers of skin ulcers, many of which were of the deep, punched-out type previously described as typical of diphtheritic ulcers. Careful clinical and bacteriological investigations were therefore made on 790 patients. Diphtheria bacilli were isolated in 174 cases; they were commoner in ulcers examined within six weeks of the original injury than in those examined later, and the proportion of the strains that were toxigenic also decreased with increasing interval between injury and examination. Staphylococci and β-haemolytic streptococci were frequently associated with the diphtheria bacilli. Ulcers yielding diphtheria bacilli were usually classed as deep (79 per cent. of 166) and usually (55 per cent.) followed some mild trauma such as a scratch or insect bite. The typical history was that the injury, instead of healing, started to enlarge and to develop a broad base covered with exudate, while the edges became oedematous and "rolled". Three-quarters of the patients had multiple lesions, and 99 per cent. of the ulcers were on the extremities. Apart from those situated on the feet, the ulcers caused little disability. Schick-positive reactions were twice as common among patients with diphtheritic ulcers as among the general population. *C. diphtheriae* was isolated from the nose or throat swabs of 19 (11 per cent.) of the 174 patients with diphtheritic ulcers; 12 of the patients had clinical diphtheria and in three of these the disease had developed while they were isolated from other patients, so that for them it is highly probable that the pharyngeal infection was derived from the patients' own ulcers.

Eleven patients were observed who had neuritis and active or healed ulcers, although in only three were diphtheria bacilli actually demonstrated in the ulcers. Since the neuritis sometimes developed as much as seven months after the ulcer, and many of the patients had not been observed as long as this at the time of writing, the overall incidence of neuritis in the ulcer cases cannot be stated. The long interval is in contrast with the six weeks commonly observed with pharyngeal diphtheria. Moreover, the distribution of the neurological signs differed from that observed with the pharyngeal infection: the first signs were commonly paraesthesiae followed by weakness of the limbs, with diminution in or loss of the deep reflexes. The protein content of the cerebrospinal fluid was raised. In the authors' experience, neuritis of this general type, in the tropics, could always be associated with the presence or a history of tropical ulcer, pharyngeal diphtheria, or sore throat.

Rest was the most satisfactory form of treatment, although the local application of a saline solution of penicillin appeared to accelerate healing. Sulphonamides had no effect. Serum treatment did not affect the ulcers, but was given to prevent the complications of possible self-infection of the pharynx.

That diphtheria bacilli may be disseminated from the skin lesions was strongly suggested by the fact that, before the tropical ulcers were recognized as diphtheritic, seven persons in the hospital developed pharyngeal diphtheria after contact with patients with skin lesions. In all reported outbreaks of diphtheritic tropical ulcers among military populations, the incidence of ulcers has exceeded that of clinical diphtheria or carriers. In the present study, the incidence of carriers in 101 men without ulcers was 0·6 per cent., whereas 7 (4 per cent.) of the men with ulcers were asymptomatic carriers. When ulcer patients were removed from contact with the rest of the men, the incidence of diphtheria among the latter decreased rapidly. The authors suggest that the marked rise

in diphtheria incidence in Europe in 1941–2 resulted from the return of German soldiers from North Africa, where diphtheritic ulcers were common. A similar rise occurred in New Zealand in 1942–3, and may be attributable to the return of men from the Pacific region.

Nasopharyngeal diphtheria is rare among the natives in the Pacific and the Schick-negative rate is high at an early age, *e.g.* 62 per cent. of 84 children under three years of age. This immunity is probably developed as a result of skin infections, which are very common among the children, and constitute an enormous reservoir of infection. *R. E. O. Williams.*

Bull. Méd. de l'Afrique Occidentale Française. 1943, v. 2, No. 3, 189–202. Les ulcères phagédéniques en Afrique Occidentale Française. [**Phagedaenic Ulcers in French West Africa.**]

In its prevalence and in the prolonged incapacitation to which it gives rise phagedaenic ulcer must be regarded as "a social disease of the first rank." The present article is divided into four chapters. In the first are general remarks on the disease and its prevalence. It is very prone to appear amongst those living in hot moist districts and wooded swamps, though it is far from uncommon in dry climates such as French Somaliland.

Returns are furnished for the five years 1938 to 1942, inclusive. The number of "consultations" for all causes at the hospitals [presumably out-patients] has remained nearly the same, with a slight tendency to rise, between 4 and 5 million (4,161,417 in 1938; 4,807,887 in 1942), but ulcer cases have increased by 36 per cent. The numbers, however, of those needing in-patient treatment have increased fourfold, from 1,840 among a total of 52,015 to 7,514 among 107,129, practically doubling the percentage, 3·53 and 7·01 in 1938 and 1942 respectively. European sufferers are few; percentages only are stated; these range between 0·23 and 1·18 per cent. for "consultations" and 0·15 and 0·44 per cent. admitted to hospital. Chapter II gives figures for the different French colonies: Senegal, Sudan, Niger, Togo, Dahomey, the Ivory coast, Guinea and Dakar. In actual numbers, in 1938 the Ivory coast (21,092) and Togo (20,016) head the list of out-patient cases, but in percentages Togo has 3·0 and the Ivory Coast 1·96. Admissions to hospital, however, were highest (821) in French Guinea, 10·5 per cent. of total admissions, the figures for the Ivory Coast and Togo being 469 and 225, or 3·01 and 3·88 per cent. respectively. Strange contrasts are observable when these figures are compared with those for 1942. In that year out-patients numbered, in Togo 25,567 (3·4 per cent. of the whole), Ivory Coast 32,070 (2·51 per cent.), Guinea 8,441 (1·93); in-patients, Togo 372 (7·08), Ivory Coast 4,111 (11·54), Guinea 573 (7·78).

The condition is particularly common among agricultural workers and those engaged in cutting wood for the railway. It is estimated that 60–80 per cent. of the disabilities among those so engaged are due to these ulcers, that the average time off duty on that account is 30 days, and the cost between 15 and 20 million francs, annually.

Chapter III is a brief one, dealing with prophylaxis. Since any wound, however small, an excoriation, the prick of a thorn, the bite of an insect, may become phagedaenic, early treatment, disinfection and protection are called for, and as preventive adequate clothing and good feeding.

Lastly, the question of treatment is touched upon. Since the suggested treatments of these ulcers is legion and the whole is dealt with in less than two pages, mere classification was all that could be given, under the two main headings of cleansing the wound, and stimulating repair by chemical, physical, biological (vitamins and vaccines) and surgical means; no details are offered.

H. Harold Scott.

Ouary & Moreau. Premières observations de traitement des ulcères phagédéniques par la pénicilline (1944). [**Treatment of Phagedaenic Ulcers with Penicillin.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 2, No. 3, 203–4.

This is a brief, preliminary account of the treatment of phagedaenic ulcers by means of penicillin, as observed by Drs. Ouary and Moreau in the native hospital at Dakar. The staff was given 30 ampoules of dried sodium penicillin, each containing 100,000 Oxford units. A solution was prepared of a strength of 15,000 units per cc. in physiological saline and kept on ice for use in the next 48 hours. From this as stock was prepared a solution containing 250 units per cc. which was applied locally by means of a swab after material had been taken for bacterial examination and the surface wiped clean. The wound was well swabbed over with the penicillin, then dressed with gauze soaked in the solution. The dressing was renewed daily. The applications were quite painless. Nineteen patients were treated thus. No details of cases are given but the authors concluded [they speak of recent ulcers only, not of those of long standing nor of those with complications]: That the penicillin "destroyed the specific association of spirochaetes and fusiform organisms"; as a rule, the ulcers were "disinfected" [presumably became organism-free] in 8 days, and small ulcers cicatrized forthwith, the larger needed grafts; relapses occurred but some were due to inadequate treatment and yielded to a second course, others were due to anatomical causes, as an underlying osteitis and sequestrum; penicillin was of service here until surgical measures could be undertaken, but, though useful as an adjuvant, it cannot replace surgical measures in such cases.

The advantages of this form of treatment are that the patients can be up and about; there is no pain nor any reaction and the method is simple. The obvious disadvantages are the necessity for storing the preparation on ice, the limited time within which it must be used, the high cost, and the waste if the whole contents of an ampoule are not needed at one session. *H. Harold Scott.*

Dostrovsky, A. & Sagher, F. **A Study on Ulcus Phagedenicum Cutis.** *Arch. Dermat. & Syph.* 1946, Oct., v. 54, No. 4, 408–24, 9 figs. [Refs. in footnotes.]

MISCELLANEOUS DISEASES.

i. Coates, A. E. **Clinical Lessons from Prisoners of War Hospitals in the Far East (Burma and Siam).** *Med. J. Australia.* 1946, June 1, v. 1, No. 22, 753–60, 6 figs.

ii. Dunlop, E. E. **Clinical Lessons from Prisoner of War Hospitals in the Far East.** *Ibid.* 761–6, 5 figs.

iii. Marsden, A. T. H. **Observations by a Pathologist during Three and a Half Years as a Prisoner of War in Malaya and Thailand.** *Ibid.* 766–9, 4 figs.

iv. Harvey, C. **Medical Aspects of the Singapore Captivity.** *Ibid.* 769–72.

v. Rose, N. H. **Some Medical Experiences as a Prisoner of War.** *Ibid.* 772–3.

vi. Stening, S. E. L. **Experiences as a Prisoner of War in Japan.** *Ibid.* 773–5.

vii. Fagan, K. J. **Surgical Experiences as a Prisoner of War.** *Ibid.* 775–6.

i. Dysentery broke out on the prison ship, and soon after the arrival in Burma from Pedang, where they had been captured, 20 out of 500 men died from fulminating amoebic infection. The meagre supplies of emetine soon being exhausted, the author performed the first operation up country, an ileostomy, for chronic amoebic dysentery in a patient who had been ill for six months

and who was having sixty bloody motions daily; the patient improved remarkably and the ileostomy was closed two years later. After some time, painful feet became very troublesome, an affected foot being pinkish blue, sweating freely, with marked arterial pulsation and severe nocturnal aching pain. At that time the diet was particularly deficient in protein, fat and vitamins of the B complex. Neurectomy of the tibial and superficial peroneal nerves was tried in one case, with relief, the nerves being found at operation to be very swollen. Working next at the 75 km. mark on the Siam-Burma railway, the author found some 300 men sick with amoebic dysentery, relapsing malaria (some cerebral), tropical ulcers, suspected cholera, corneal ulcers and scrub typhus, but apart from a little quinine there were no drugs available. Although ill with typhus he was then moved to Kohn Kuhn camp, at the 55 km. mark, to assist the two doctors and six medical orderlies who were looking after some 1,800 patients whose only accommodation consisted of eight large and one small *atap* (palm leaf) covered bamboo huts without beds or bedding; the small hut was for infectious cases, was known as the "dead house", and contained 100 dysenteric patients. Post-mortem examination of 12 cases of amoebic dysentery showed sloughing of the lower part of the colon, ulceration and sometimes gangrene up to but never beyond the ileo-caecal valve, occasionally adherent masses in the right iliac fossa and perforation. The Japanese refused to issue emetine on the grounds that without microscopical diagnosis it was impossible to confirm that amoebic infections existed, and they further insisted that the term amoebic dysentery be deleted from some 30 death certificates and replaced by the term hill diarrhoea. Later a microscope and a bottle of extract of ipecacuanha were obtained; from the extract a Dutch medical orderly prepared 150 doses, each of 1 grain, of emetine which used in courses of 5 injections produced a dramatic arrest of haemorrhage and tenesmus.

As 1943 wore on, pellagra became apparent, and was characterized by a sore fissured tongue, angular stomatitis, anorexia, dysphagia, persistent watery diarrhoea, and occasionally a typical rash. Autopsy showed a shrunken heart, liver, spleen and kidneys, a diaphanous bowel and a small thin-walled stomach; in some cases the brain was shrunken with convolutional atrophy and secondary hydrocephalus, such patients having mental symptoms before death. Nicotinic acid, had it been available, would not have been effective as the changes were irreversible. Fat and protein were the real deficiencies, and many patients were saved by meat clandestinely obtained from the local villages at night. Nutritional oedema was often associated with pellagra. It was first thought to be beriberi, but attempts to relieve it by vitamins failed while there was a remarkable response to meat plus deprivation of fluid. The term beriberi was, however, often used in death certificates, as it was one of the few terms the Japanese could appreciate.

Ulcers of the leg were very common. If the disease and the patient were in equilibrium there would be a circular ulcer with slightly undermined edge and a sloughing base bounded by, but never penetrating, the deep fascia; the site was often malleolar or on any part of the lower leg, but might be anywhere, and was often determined by some mild trauma. Foments, curettage, iodoform dressings and rest produced suppuration and healing. In patients forced to work, suffering from frequent malaria, malnutrition and exhaustion, the ulcers spread, penetrating the deep fascia, muscle, periosteum, tendon sheaths and blood vessels; there was a thin watery foul-smelling discharge without pus formation, and gangrene became universal. Excision led to cure in about 60 patients, and widespread removal of tissue, including the *Tendo Achillis*, peronei, anterior and posterior tibial tendons resulted in surprisingly little disability. In some cases the joints became eroded, pain was excruciating, there was no morphine, and the patients yearned for relief by amputation.

When meat was given, even large ulcers began to suppurate, quietly formed sequestra, and when the sequestrum was removed finally healed. The Dutch did not suffer as much from ulcers as did the British and Australian troops. Remarkable bamboo pylons and crutches were improvised for the limbless patients.

In January and February 1944, a new camp, the Nakompaton Sanatorium, was constructed 35 miles from Bangkok, for 10,000 chronically sick and disabled European prisoners from the Burma-Siam railway. The equipment was minimal, and the medical staff allotted by the Japanese numbered only three medical officers and 13 medical orderlies per 1,000 patients. Food was issued on the following basis : outside workers, rice 600 gm., meat 150 gm., vegetables variable ; inside workers, including medical staff, rice 500 gm., meat 100 gm. ; patients, rice 400 gm., meat 50 gm. on the Japanese principle that the sick should receive little or no food. Red Cross supplies of drugs arrived in the middle of the year and were invaluable, providing enough emetine for a half course of treatment for 250 of the 1,346 patients suffering from amoebic dysentery. A demonstration that scrotal dermatitis was heralding an outbreak of pellagra induced the Japanese to issue rice polishings, 25 gm. per man per day, while clandestine trading, raising of ducks and pigs also helped. Many cases labelled beriberi were shown to be examples of effort syndrome. Blood transfusions, with defibrinated blood which gave surprisingly few reactions, was found a most useful contribution to the healing of all sorts of conditions. Amazing improvisations were devised in the pathology department. Sexual perversions were rare, and no murders and only two suicides were recorded in 18 months, while the number of mental patients under restraint never numbered more than 30. Aseptic surgery was not possible, but 896 major operations were satisfactorily performed. Naked hands were scrubbed in several changes of water and then immersed in alcohol made in the camp, gowns were sterilized in a home-made autoclave, instruments were boiled and the skin was cleansed with alcohol. Interrupted cotton sutures without tension and as few catgut ligatures as were compatible with haemostasis were employed. Spinal anaesthesia was used for all operations below the nipple and usually local anaesthesia elsewhere, as there was no ether and very little chloroform. Naked hand technique was found unsuitable for exploring the abdomen, adhesions resulting from infection from the sweating hand. Renal calculi were particularly common, there being some 65 cases at the time of release. Physiotherapy proved invaluable, and the department with its attached workshops provided artificial limbs ingeniously made from odds and ends for 170 men. Morale was maintained at a high level, and in May 1945 the underground news service, operated at great risk and with great courage, made the camp aware that release was imminent. The overall mortality figure of 3 per cent. for the camp is a tribute to the medical staff and their splendid work.

ii. An allied general hospital, captured in Java in March 1942, was brutally dissolved and its medical stores ruthlessly confiscated. Despite protests, the patients were marched to an overcrowded gaol where medical arrangements were negligible, rations deplorable and no recognition was given to medical personnel. Within a few months deficiency diseases appeared, the early symptoms being angular stomatitis, glossitis, pigmentary changes and a dry scaly skin, followed later by scrotal dermatitis ; there was later opportunity to prove that 6 to 8 mgm. riboflavin daily rapidly brought about improvement of the condition. Painful feet became troublesome ; there was usually marked sweating with a clammy feeling, the deep muscle reflexes were hyperactive, with sometimes clonus and rarely spastic diplegia. At this time dimness of vision was also noticed, especially affecting the centre of the visual field.

The author was then sent to look after a working force on the Burma-Siam railway, in the neighbourhood of the Kwa Noi river. Conditions were very bad. Clothing and boots rapidly wore out and were not replaced, the rations were inferior, and accommodation consisted of hovels of bamboo which provided little protection against the monsoon weather. Exhortation and savagery were used to exact work from the wasted and diseased men, some of whom staggered out supported by sticks or were carried to the parade ground, as the Japanese required a fixed number of men to be produced daily for work under threat of deprivation of food and water. Drug supplies were negligible.

Numerous outbreaks of cholera occurred, particularly during the humid monsoon season; at Hintok camp of 1,000 men there were 150 cases, of which 63 were fatal in one outbreak. The cases were typical and severe; an early sign was a ringing noise in the ears, weakness and faintness, with sometimes death within a few hours. The Japanese were terrified and anxious that the affected men should die quickly, so that they even shot the sick. Men stricken at work were not allowed to be carried in by their fellow workmen but had to lie out until carriers were sent out to them. Accommodation for the patients was inadequate, the bedding was deficient, the men could not be kept dry and they lay on rough bamboo covered by their soaked rags of clothing, the whole area soon becoming contaminated by their uncontrollable vomiting and purging. Anuria was a disastrous complication and was not affected by massive administration of fluid. Improvised stills were constructed and infusion apparatus made from such make-shift materials as drilled bamboo thorns used as cannulae; in severe cases up to 20 pints of saline were given daily, the first 4 to 6 pints being administered fairly quickly, after which an attempt was made to balance the fluid output and intake. The mortality averaged more than 50 per cent., varying from about 40 to 80 per cent. in different outbreaks; the dead were disposed of by massive cremation. All patients recovering from cholera developed severe protein oedema after the active symptoms had subsided.

Dysentery was the greatest immediate cause of death among prisoners in Burma and Siam, and in the author's area was responsible for between one-quarter and one-third of all deaths. The most serious outbreaks of bacillary dysentery occurred during the first year, and later some resistance seemed to be acquired; where available sulphaguanidine gave splendid results, and quite small doses of sulphapyridine also proved very effective. The majority of the cases of chronic dysentery were ultimately proved to be due to amoebic infections, and in some cases mixed infections occurred. Amoebiasis was often of appalling severity, and there was an acute shortage of emetine. The florid cases had cellulitic swelling and tumour formation, not infrequently associated with patches of gangrene spreading out to the peritoneal coat and causing death from peritonitis or actual perforation, usually about the caecum and ascending colon, but spread to the ileum was negligible. Chronic cases often failed to respond to emetine, and in these surgery was indicated. Ileostomy, some 18 inches from the ileo-caecal valve, was the most valuable measure, as freedom from infection rendered it a safe area and the complete diversion of faeces ensured complete rest for the bowel. It was important to guard against dehydration in the early post-operative stage, but there were only 3 deaths out of 14 cases, and most patients regained health and were enabled to carry on a surprisingly active existence. Caecostomy and appendicectomy were also performed, and healing after the later operation was excellent provided the small arterial branch at the base of the appendix was preserved; sometimes in the absence of emetine, disastrous infection of the abdominal wall followed.

During the latter part of 1943, all camps contained hundreds of men suffering from serious tropical ulcers ; at Tarsau there were 700 cases among 2,500 men. The Dutch troops, who included a high percentage of Eurasians, suffered much less than did the United Kingdom and Australian troops. After some months in the jungle septic ulcers developed at the site of some slight trauma. Later the more disastrous tropical ulcers were seen, with a rapidly spreading foul gangrene and massive necrosis surrounded by a zone of inflammatory reaction ; in a week or two the ulcer might become the size of a saucer or larger, spread through the fascial planes and cause necrosis of bone and tendon. Secondary haemorrhage and suppurating phlebitis often occurred. Sometimes ulcers were multiple, giving rise to widespread phagedaena, severe toxaemia, pain, misery and death. In the less severe cases, the continuous smarting irritation lead to muscular spasm with, finally, contractures of the limb. Sulphonamide drugs applied locally had little effect, and strong cauterizing agents were more effective, but iodoform was the most valuable local application, especially when combined with curettage or excision followed by grafting. Sequestra formed in many cases where there was deep necrosis, and required sequestrectomy. Amputation was necessary in severe cases of ulcer ; the average mortality was 50 per cent., but death was often delayed for weeks or months and was associated with water-logging through nutritional oedema, the mortality immediately following operation being only about 10 per cent.

iii. The main dietary deficiencies were as follows : fat, at all times grossly deficient ; protein, the daily absorption of which was only about 32 gm. ; vitamin B complex, vitamin B_1 being deficient for the first two years, while vitamin B_2, including riboflavin and nicotinic acid, was deficient throughout the whole period. The effects of these deficiencies were seen in loss of weight with mental apathy, lassitude and low blood pressures. Hypoproteinaemia occurred with its usual effects and also resulted in slow convalescence from diseases which had involved much loss of weight. There were also numerous cases of beriberi and pellagra. Amblyopia was usually attributed to deficiency of some factor of the vitamin B complex, but it was suggested that it might be due to deficiency of fat. There was also an increased susceptibility to disease as evidenced by the high incidence of tropical ulcers. An altered clinical reaction to disease was suggested by the low grade pyogenic infections, such as those of the prostate and bone, that occurred, by the multiple relapses of malaria and by the relapse of dysentery that followed resumption of work by patients. The effects of disease were increased by avitaminosis, especially in dysentery when the diarrhoea increased the malabsorption of vitamins.

The use of defibrinated blood provided a simple and satisfactory means of blood transfusion. In anaemia, transfusion appeared not only to add cells but also to stimulate the bone marrow to the production of new erythrocytes, presumably by increasing the nutrition of the marrow.

There was a curious outbreak of hepatitis in 1945, characterized by low fever persisting two to three months, anorexia, tenderness over the liver, sometimes palpable enlargement of the liver and usually at some time jaundice which was often very slight. There were no fatal cases, but a piece of liver obtained at an operation showed periportal fibrosis with infiltration of the portal tracts by small round cells. The condition was thought to be due to the low protein diet with a low vitamin B content, probably combined with bacterial infection.

In the examination of numerous amoebic stools for cysts, the author found that six consecutive examinations of the stools from each patient resulted in the detection of about half the cases in which actual infection was present ; one examination detected about 20 per cent. of the cases, two examinations about 30 per cent., and three examinations about 37 per cent. For the

diagnosis of suspected chronic amoebic infections and for test of cure, he thinks sigmoidoscopy important, with microscopic examination of scrapings from all doubtful ulcers.

iv. The rapidity of the fall of Singapore resulted in the captured force having a large number of skilled medical persons, and large quantities of drugs, instruments and equipment; the position would therefore not have been so sombre had it not been for the ever present deficiency of food.

The outstanding problem at first was the dysentery epidemic, but owing to the complete co-operation of all units in camp hygiene it did not assume the proportions originally feared. In treatment, sulphapyridine was found extremely valuable when supplies of sulphaguanidine were not available.

Deficiency diseases eclipsed all other medical problems. Beriberi appeared within six to eight weeks, but in order to induce the captors to increase the diet it was deliberately overdiagnosed, all cases of oedema of the feet or of sudden death being so classified. Other deficiency diseases followed, and because of the recognized importance of green leaves and grasses as sources of riboflavin, improvised methods for the extraction on a large scale of grass and green leaves were devised, so that soon 50 gallons of grass extract were being prepared daily with an estimated riboflavin content of about 5 mgm. per pint. There was an outbreak of diphtheria with remarkable skin manifestations. The value of X-ray examination of the chest appeared demonstrated, since the Australian troops who had been so examined on recruitment developed no tuberculosis until a year after captivity, whereas the British had 30 cases within the first six months.

In May 1944, the hospital was moved to Kranji, 25 miles across the Island and near the Jahore Causeway. Here 1,200 patients were accommodated in palm leaf huts, but owing to the large population at Changi and the breakdown of transport, more sick were finally dealt with at Changi than at the new hospital site. Rations at this time showed a gradual diminution in calorific value, but an improvement in the thiamin/non-fat calorie ratio, chiefly because of reduction in rice and increase in green vegetables; in other words the diet was lower but better balanced. This resulted in a general decrease in body weight and a decrease in deficiency diseases. There was also a decrease in malaria owing to the excellent work of the anti-malarial control group, who were permitted to make excursions twice weekly for oiling and drainage work in the vicinity of the camp. There were occasional outbreaks of dysentery, but acute diarrhoea almost always responded immediately to a short course of sulphaguanidine (10 gm.). Amoebic infections were treated with a short course of emetine (4 gr.) when the drug was available; in its absence, enemata of acriflavine were found of benefit. Chest conditions did not do well at Kranji, and many patients, especially the asthmatical, had to be returned to Changi. Red Cross food supplies gave a great psychological stimulus, although the amounts were not enough to have any real physical effect. Educational features and a theatre were improvised, lectures were organized, and ward rounds and medical society meetings were held; all these welfare activities contributed greatly to maintenance of morale, as did the provision of a daily news bulletin, often obtained at great risk.

v. When the author arrived at a 500-bed hospital, catering for 55,000 prisoners (40,000 Russian, 9,000 British and 6,000 French) in Upper Silesia, all the prisoners showed evidence of starvation, protein oedema being the rule. Lice and bugs were ubiquitous, beating of the sick was common, and the Germans made a definite attempt to exterminate the Russians. The first task, therefore, was to gain control of the internal organization of the hospital.

Despite the language difficulty, the keenest and most alert prisoners were trained as orderlies, dressers and assistants. Patients were segregated into wards

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according to diseases. Red Cross parcels, provided for the British but not for the Russians, were shared out and saved inumerable lives. A garden was started and subscriptions from the British prisoners were used to purchase drugs, food, instruments and comforts. A sports field was constructed as well as work rooms, laundry and facilities for welfare activities.

The medical work was performed by a team of six medical officers, of mixed nationality ; on the surgical side during 15 months, 375 major operations were carried out, including 83 appendicectomies, 41 herniotomies, 2 gastrectomies, 7 craniotomies, in addition to numerous other procedures, without a death among the British patients.

vi. After many hours in oil-covered water, over 300 men were crowded into one hold of a Japanese prison ship and were taken to Java. Dressings, medicines and food were all scarce, and, three to four months after capture, the prisoners began to show evidence of deficiency diseases. Some developed oedema and some pellagra, the latter being accompanied by an intolerable itchy weeping eczema of the scrotum. Later the prisoners were transferred to Japan, where conditions were equally deplorable. Of one ship-load of 1,000 prisoners from Singapore, 80 died from starvation and dysentery before reaching Japan, 200 died soon after arrival, and 40 per cent. were dead within 3 months of arrival. In a camp on the north coast of Honshiu Island, diarrhoea soon became almost universal. Deficiency diseases were common ; of 300 men at one time, 209 were suffering from beriberi, 156 from pellagra, 120 from defective eyesight and 8 from nerve deafness. The cases of beriberi had oedema of mild or severe degree and could not be distinguished from starvation oedema ; the absence of reflexes was not thought to be of significance in the differentiation. Bradycardia was the rule, a pulse rate below 40 being common ; a sudden rise in rate was of bad prognostic significance, although sometimes death occurred with persistent bradycardia. Pulse pressures were always low. Treatment of infections with sulphonamide drugs often precipitated the onset of beriberi, usually after a latent period of about a week, probably because of destruction of intestinal bacteria and consequent inhibition of vitamin synthesis. Thiamin in large doses had only slight effect on the oedema, and the most successful method of treatment was restriction of fluid intake. The prominent symptoms of pellagra were glazed tongue and angular stomatitis, dark fish-scale skin, eczema of the scrotum, defective vision, painful feet, diabetes insipidus and polyuria, and mental deterioration. In their efforts to obtain relief from painful feet by cooling, many men contracted frozen and gangrenous feet, analogous to trench feet.

vii. Facilities for dealing with surgical casualties in Singapore during the first few months after its capture were reasonably good as there was a considerable amount of equipment, and the main difficulties arose from malnutrition and infection. Later, in Siam, these difficulties became even more the prominent problem. Rations were worse, especially as regards fat, protein and vitamin content, the region was highly malarious and the indigenous population nearly all carried amoebic infection. An epidemic of cholera killed 25 per cent. of the camp strength in 6 weeks, and acute phagedaenic ulcers appeared three weeks after arrival in Siam. The ulcers developed sometimes spontaneously as a small vesicle on an indurated inflamed base, or they followed some minor scratch or cut. In the severer cases, progressive and extensive destruction of the tissues occurred, with intense pain and toxaemia. The best treatment appeared to be early excision of the necrotic tissue, but once the deep fascial barrier was penetrated secondary operations such as excision of necrotic tendons and sequestrectomy were often necessary, while in the advanced stages amputation was the only treatment even though its mortality was high. Experience demonstrated that necessary surgery can be performed in any circumstances provided fuel

and water are available and there is an adequately trained staff accustomed to improvisation. The Steinmann pin was found of great value in the treatment of fractures of the lower limb under primitive conditions; its simplicity and portability make it invaluable where no plaster, strapping or bandages are available. The author also found chloroform a safe and economical anaesthetic under the conditions of tenuous supply lines. *F. Murgatroyd.*

MARRIOTT, H. L.; HILL, I. G. W.; HAWKSLEY, J. C.; BOMFORD, R. R. **Medical Experiences of the War in the South-East Asia Command. I–IV.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, June, v. 39, No. 6, 461–79, 1 chart. Discussion 479–84 [HOOD, A.; BENNET, J.; BENNET, E. A.; MANSON-BAHR, P.; MACGREGOR, R. B.; MURGATROYD, F.; BIGGAM, A. G.; NAPIER, L. E.; MARRIOTT, H. L. (in reply)].

Dr. H. L. MARRIOTT said that the primary lesson was that in warfare in tropical regions medical considerations are of pre-eminent importance. In 1942 and 1943 units of the Eastern Army sometimes had sickness rates so high that practically every man had gone down with sickness and been admitted to hospital inside 2 months. Even in 1944 the admission rate was 1,000 per 1,000 per annum and the ratio of casualties from sickness to casualties from wounds, despite much heavy fighting, was 19 : 1, while in 1943 the ratio had been 121 : 1.

Malaria was the greatest problem and caused about half of all sickness. Suppressive mepacrine, 0·1 gm. daily, caused a remarkable drop in the incidence of malaria, and the value of DDT was becoming demonstrated in the closing stages of the Burma campaign. Avoidance of native areas at night and personal protection by nets, clothing and repellents were also important. Diarrhoea and dysentery, causing a hospital admission rate of about 100 per 1,000 per annum, were the second greatest trouble; the proportion of cases showing *E. histolytica* was about 20 per cent. It seemed that water might be the chief mode of spread for both bacillary and amoebic dysentery; it is essential that some method of water purification shall be found which will kill amoebic cysts. The most useful measure in diminishing the spread of bacillary dysentery was very prompt use of sulphaguanidine, and mass treatment with sulphonamide drugs was also the answer to high incidence of carriers in units. Sprue and sprue-like syndromes were also much in evidence. Anaemia was common in Indian troops, the primary cause apparently being blood destruction from chronic malaria; a contributory factor was the low meat-content of their diet as tinned beef was unacceptable to them since Indian scruples of religion or custom require goats or sheep killed according to Hindu or Muslim rites. Plans were begun during the war for the large scale manufacture for the Indian Army of canned meat certified by religious leaders as having come from animals killed in the proper manner; such plans should now be developed. Scrub typhus was a worry from the autumn of 1943 onwards, about 1 man in 100 contracting the disease. Skin diseases, the chief of which were intertrigo, fungus infections, prickly heat, scabies, and impetigo, caused a hospital admission rate per annum of 1 man in 20; the admission rate for venereal diseases was about the same.

The speaker thought that the standard of disease prevention was much too low, and that it was absurd that less than 5 per cent. of the medical personnel were engaged in purely preventive work while most of the rest were engaged in treating diseases which in many instances need not have occurred if known knowledge had only been applied; he suggested that an allocation of 30 per cent. of the personnel to prevention would not have been excessive. Furthermore, education in tropical hygiene should be a part of the whole Army's routine training, and one of the most important sections of a medical directorate should be a section for expert propaganda of hygiene.

Early and adequate treatment of disease is of the greatest importance. Malaria can be controlled in 2 to 3 days, bacillary dysentery in a few days, skin diseases can be cured quickly if tackled early, gonorrhoea can be cured with penicillin in 24 hours and syphilis in a week; these conditions accounted for three-quarters of the total hospital admissions. He suggested, therefore, that for future wars in the tropics the organization should provide to treat 75 per cent. of medical casualties in light mobile forward medical units attached to corps or divisions, while provision of base hospital beds, outside operational areas, should not be for more than 25 per cent. of the expected cases of sickness. Bearing on this a tradition should be created that fosters the importance of the R.M.O., and a reform, basic to such a tradition, is that at least half of all R.M.O.s should be majors.

Dr. Ian G. W. Hill, remarking on the lowered trend of sickness rates during the latter part of the Burma campaign, said that the lessened incidence of dysentery and diarrhoea appeared undisputedly linked with the use of sulphaguanidine, while every effort was made to treat cases as far forward as possible. The abrupt fall in the incidence of malaria between October and November, 1944, coincided with the enforcement through staff channels of mepacrine suppression; as a corollary there was a marked drop in the incidence of cerebral malaria and blackwater fever. The low incidence of smallpox among large bodies of men exposed to high risk of infection from Burmese villagers and refugees at the time of the Irrawaddy crossings, was a tribute to the efficiency of vaccination. Immunization against cholera was also practised, but control by hygienic methods probably contributed predominantly to suppression of the disease. Scrub typhus was found along the jungle tracks around Imphal and in the valley of the Kaldan; the fall in its incidence in the early months of 1945 was probably seasonal, although by that time measures of personal protection by dibutylphthalate were in use.

Dr. J. C. Hawksley said that the state of the Japanese prisoners taken in July and August 1945 showed how completely their medical services had broken down; over 80 per cent. had malarial parasitaemia, and diarrhoea was rife. The principal problems among the prisoners of war and civilian internees in the Japanese hands were chronic diarrhoea, malaria, beriberi and straightforward starvation; medical officers sent forward for the relief of prisoners of war in circumstances where conditions are unknown should contain a proportion of senior officers who are medical and hygiene specialists, and not only junior officers. In view of the increasing complexity of modern therapeutics he thought that an army in the field needed an adviser in pharmacy with wider and more up-to-date knowledge than can be expected from either a consulting physician or an ADMS in charge of medical stores.

Dr. R. R. Bomford stated that the low sickness rates, together with efficient air evacuation, enabled the medical services to meet the commitments of the last month or two of the 14th Army's campaign with an actual forward bed cover of 2·7 per cent. for British troops and 1·7 per cent. for Indian troops, instead of the 7 per cent., or more, generally considered necessary in tropical warfare. Dealing with the prisoners of war and internees on Singapore Island he said that there were approximately 36,000, of whom between 5,000 and 6,000 were evacuated through medical channels. The main deficiency diseases during the occupation were those attributed to deficiency of vitamin B complex, low plasma-protein oedema, malnutrition diarrhoea, and anaemia. He thought the association of retrobulbar neuritis, 8th nerve deafness and spastic paraplegia, recently regarded as a syndrome, was probably only a coincidence. Malaria was not as serious a problem in Singapore as in Siam; dysentery, especially amoebic on account of the scarcity of emetine, caused much illness, and

diphtheria, more than half of which were cutaneous cases in some outbreaks, was a serious problem.

In the subsequent discussion, Lieut.-General Sir Alexander HOOD, referring to the difficulties encountered, said that we were not equipped nor prepared either with men or with materials to fight more than one war at a time ; priority had first to be given to the Middle East, then to North Africa and Italy, later to North-West Europe, and finally to the 14th Army. He agreed on the importance of hygiene officers, but pointed out that what is required is to inculcate into the Commanders in the field the necessity of hygiene measures before they can be carried out, and that this was one of the great achievements of Brigadier Hamilton Fairley's work in Australia.

Dr. E. A. BENNET said that many patients, apparently suffering from psychiatric illness, were found to have some physical disease, particularly malaria, and he emphasized the need for the complete physical examination of patients with psychiatric symptoms. The campaign in Burma was conducted in difficult country necessitating a special psychiatric organization ; each division was provided with a small psychiatric unit, and this worked so well in practice that it is worthy of close consideration in the medical planning of a campaign, especially in tropical countries.

Sir Philip MANSON-BAHR said that the majority of the ex-internees from Eastern prison camps suffered from oedema which was diagnosed in the British Zone as wet beriberi but by the Dutch as hunger oedema. He considered the latter to be the correct diagnosis, as so many of the patients recovered rapidly without residual nerve involvement.

Dr. R. B. MACGREGOR thought that both beriberi and hunger oedema occurred, sometimes at the same time, sometimes separately, sometimes in different individuals, or in the same individuals at different times. In fact, the most striking feature was the different reactions of individuals exposed to precisely the same conditions of privation and hardship. He also drew attention to the " oedema of plenty " which so frequently supervened when the prisoners were released and were given plentiful food again.

Dr. F. MURGATROYD also remarked on this latter form of oedema which he had observed in patients without grossly obvious cardiac or neuritic signs and without low plasma protein levels, and he wondered whether it might be correlated with capillary or renal defects resulting from malnutrition.

General A. G. BIGGAM emphasized the importance of preventive medicine in tropical combat areas. Referring to the high incidence of amoebic dysentery he said that although the treatment of amoebic dysentery was not entirely satisfactory yet treatment with penicillin and sulphonamide prior to specific anti-amoebic drugs had entirely changed the outlook in chronic infections and that it was seldom that cure was not now effected.

Dr. L. E. NAPIER was horrified to hear that it was the end of 1944 and the beginning of 1945 before principles of malaria prevention that had been laid down 10 years before were applied effectively. Admittedly the suppressive dose of mepacrine used pre-war was too small, but it should not have taken very long to adjust to the new circumstances ; yet in the beginning of 1944, although the campaign had been going on for about 2 years, there was still a very high incidence of malaria. He suggested that instead of dropping senior medical officers by parachute, as had been suggested, the young officers should be taught a little more tropical medicine. *F. Murgatroyd.*

EARLE, K. V. **Penicillin in the Treatment of Tropical Pyomyositis.** *J. Trop. Med. & Hyg.* 1946, Dec., v. 49, No. 6, 111–12.

" (1) The successful treatment by penicillin in two cases of tropical pyomyositis is described.

" (2) The superiority of penicillin over sulpha drugs in the treatment of this disease is tentatively indicated."

RADOVICI, A. Sur une épidémie de lathyrisme. [**An Outbreak of Lathyrism.**] *Bull. Acad. Méd. Roumanie.* 1945, v. 17, Nos. 1/3, 77–86.

In the winter of 1942–43 rumours began to spread of an " epidemic of paralysis " among the inmates of a concentration camp at Vapniarka. Communication from outside, either personally or by writing, was prohibited and it was surmised that the disease was beriberi. Soon after, however, a lady doctor was among those sent to the camp and she observed that the paralysis was of a spastic type. Further investigation revealed that the diet consisted of dried peas of poor quality, boiled in water and a slice (100–200 gm.) of bread made with oat-flour, potatoes and straw. The " Vapniarka peas " proved to be *Lathyrus sativus*. An interview was obtained with the Minister of Public Health and this information was given to him, but no answer was forthcoming and the author does not know if anything remedial was undertaken.

Among the 1,200 persons detained 600 were attacked ; they had been brought to Rumania on September 16th, 1942, and nearly half the number had for some time previously been compelled to work hard, on an inadequate diet, and several showed signs of pulmonary tuberculosis. The diet prior to their removal had consisted of 200 gm. of *Lathyrus* and a thin slice (80 gm.) of bread, and on arrival they were suffering from hunger oedema and some died before the signs of lathyrism appeared. Such symptoms began to manifest themselves in October–November 1942—muscular cramps and frequent micturition—and the first case of spastic paraplegia was observed on December 27th. By January, cases numbered 600 and 35 per cent. had spastic paraplegia. Those who escaped were such as were able to buy other food or those receiving parcels of food from relatives outside. Towards the end of January 1943, other food was substituted for the *Lathyrus* ; no new cases occurred and those afflicted began to improve ; of the 650 sick in December only 65 presented symptoms in the following February, and only 51 suffered from paraplegia or paraparesis. Later a few of them relapsed ; the cause of this could not be ascertained and the only surmise was that the work was too heavy, the food inadequate and the weather humid. In practically all, cramp, especially of the leg muscles, and frequent micturition preceded the paraplegic or paretic symptoms ; hemeralopia was another symptom " common to all ".

Treatment comprised administration of brewers' yeast, vitamin B, hyposulphite and nitrite of sodium, calcium, acetyl-choline, antispasmodics such as luminal and papaverine, and liver extract. Physiotherapy and ionization gave poor results, but some amelioration seemed to follow injection of Pelacotine [this is not defined, nor is the dose stated], vitamin B_1 and liver extract.

H. Harold Scott.

GENERAL PROTOZOOLOGY.

PRATT-THOMAS, H. R. & CANNON, W. M. **Systemic Infantile Toxoplasmosis.** *Amer. J. Path.* 1946, July, v. 22, No. 4, 779–95, 6 figs. on 3 pls. [23 refs.]

The case described is that of toxoplasmosis in a new-born infant, which proved fatal on the fifth day of life. It is the first case to be recorded from S. Carolina and probably the first from the south-eastern States. The child was the first of the parents, who are both in good health. The infection appears to have commenced just before or just after birth. Toxoplasmata and accompanying lesions were found in the brain, spinal cord, heart, lungs, adrenals,

stomach, pancreas, and diaphragm. The infection was evidently of short duration and was in its invasive stage. There was complete absence of the calcification which is characteristic of those of longer standing. This is the 21st case of toxoplasmosis proved by necropsy. Fifteen of these were in infants, 2 in children and 4 in adults. In a very useful table, details of the 21 cases are set out in a comparative manner. *C. M. Wenyon.*

GENERAL ENTOMOLOGY.

MUESEBECK, C. F. W. **Common Names of Insects approved by the American Association of Economic Entomologists.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 427–48.

BRISTOWE, W. S.; MELLANBY, K. **Man's Reaction to Mosquito Bites.** [Correspondence.] *Nature.* 1946, Nov. 23, 750–51.

i. The writer refers to Dr. Mellanby's previous note [this *Bulletin*, 1947, v. 44, 240] and points out that since biting insects have a preference for different hosts, it would be important to discover whether those who claim that they have never been bitten by any insect are giving accurate evidence, or whether they have reached Stage IV described by Dr. Mellanby and do not suffer from any bites which they may have received. The writer further suggests that if the results of tests indicated such a course, it might be possible to develop some method of inoculation which would make man unattractive to biting insects.

The writer makes the startling statement that "in the world as a whole more premature deaths are probably brought about annually by the direct and indirect results of insect bites than from any other cause", and goes on to point out the discomfort, apart from the danger, of many insect bites and the vast sums expended in the destruction of biting insects and in the control of diseases caused by them.

ii. Dr. Mellanby, in reply, quotes experiments in which *Aëdes aegypti* and *Anopheles maculipennis atroparvus*, when they were hungry and had no alternative source of food, appeared to feed equally on every person whom opportunity presented. In the more difficult experiment of giving mosquitoes a choice of individual on which to feed, no consistent preference or avoidance of any particular persons were noted.

He considers that the explanation of different individual attraction is to be found in differing reactions to the bites; for example, the delayed reaction, in a person experiencing it, may suggest to him that every bite which is itching on a particular occasion has been recently inflicted, though such results have in fact followed attacks on the preceding 3 or 4 days. The delayed reaction to bites is much more troublesome than the immediate, and persons in Stages I and II are more conscious of a mosquito nuisance than those in the late stages.

Experimental evidence tends to minimize the importance of individual attractiveness, and although Dr. Mellanby believes that this factor may be found to exist, he does not consider that it is likely to be an absolute one or important enough to indicate a method of control.

H. J. O'D. Burke-Gaffney.

RIBBANDS, C. R. **Man's Reaction to Mosquito Bites.** [Correspondence.] *Nature.* 1946, Dec. 21, 912–13.

This letter refers to BRISTOWE's query [see above] regarding individual attractiveness to mosquitoes.

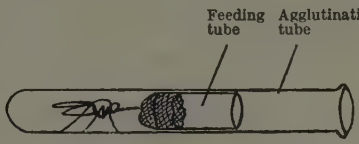
The author was able to show experimentally by deterring mosquitoes from huts by means of minute quantities of pyrethrum, that about 250 per cent. more females of *A. funestus*, *A. gambiae* and *A. melas* were attracted to three particular men than to a fourth ; and the reverse observation was noted over a period of three months in which sleeping duties were in rotation. He was also able to prove variation in attractiveness of the same person at different times. For example, the least attractive of three men suddenly became more attractive for 8 out of 9 days, and in this period attracted 186 *A. melas*, as compared with 77 for his nearest rival. The author quotes DE MEILLON [this *Bulletin*, 1936, v. 33, 245] who showed that thorough deodorization with soap and water considerably diminished attractiveness to *A. funestus* : but he does not consider that this sufficiently explains present results which he believes to be due to personal physiological variations.

Whilst there are probably wide differences between relative attractiveness of persons of different habits, the author, who knows of no proved case of immunity, considers that claims of it sometimes made are erroneous.

H. J. O'D. Burke-Gaffney.

MATTINGLY, P. F. **A Technique for feeding Adult Mosquitoes.** [Correspondence.] *Nature.* 1946, Nov. 23, 751, 1 fig.

The author starts with a single mosquito in an agglutination tube, which is kept horizontal. Into it he slides a short length of glass tubing, the " feeding tube ", of such diameter as to make an easy fit. The inner end of the feeding tube, next the mosquito is plugged with gauze, on which defibrinated blood or some such food is placed with a pipette.



Illustrating technique for feeding single adult mosquitoes.
[Reproduced from *Nature*.]

It is found that the age of the mosquito has an important influence on its feeding ; for instance, under West African coast conditions *Culex fatigans* feeds most readily when 72 hours old, *A. aegypti* at 60 hours.

The technique is obviously simpler than those involving the use of a pipette. For some purposes, especially if one must work with single insects, it is preferable to feeding in a cage from an open surface of gauze or through a membrane.

With this method, the author can infect single insects with blood containing virus ; he has, for instance, infected a male *A. aegypti* with a yellow fever virus, and recovered virus a fortnight later. He has also used the method in physiological studies, giving his insects various fractions of blood, or milk, solutions of sugar and so forth. *P. A. Buxton.*

WOODHILL, A. R. & PASFIELD, G. **An Illustrated Key to some Common Australian Culicine Mosquito Larvae, with Notes on the Morphology and Breeding Places.** Reprinted from *Proc. Linnean Soc. New South Wales.* 1941, v. 66, Pts. 3–4, 201–14, 11 figs. [14 refs.]

The terminal segments of the fourth stage larvae of nine common Australian culicines are figured and described and a key is given for their identification.

The species are *Aëdes aegypti*, *A. notoscriptus*, *A. alboannulatus*, *A. vigilax*, *A. concolor*, *A. alternans*, *Megarhinus speciosus*, *Culex annulirostris* and *C. fatigans*. *H. S. Leeson.*

BONNET, David D. & WORCESTER, D. J. **The Dispersal of *Aedes albopictus* in the Territory of Hawaii.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 465–76, 1 fig. [30 refs.]

After reviewing the literature on the methods used in determining mosquito flight range, the authors then describe the methods they employed in studying the dispersal of *Aëdes albopictus* in twelve release-recapture experiments made in Oahu, Hawaii, from August to November 1944.

The mosquitoes were bred in the laboratory and released at four release and recapture stations after they had been dusted with a mixture of 50 parts flour and 1 part dye. The dyes used were Auramine "O", Pyrazol Red, Gentian Violet, Malachite Green, Methyl Orange, Toluidine Blue, Pyrazol Violet and Chloramine Red; all were successful except the last-named. Recapturing was done at the release points and at 29 other places. Experience showed that 15 to 20 minutes collecting by Matheson's aspirator was the practical limit; it was possible for one man to collect 200 mosquitoes in an hour. Carbon tetrachloride vapour was used to kill the mosquitoes which were first identified and then dipped into the dye solvent, which consisted of 70 per cent. alcohol, 3 parts; glycerine 1 part; and chloroform 1 part.

The total number of marked *Aëdes albopictus* released was 7,100; the total captured was 29,567 of which 183 were marked specimens. The percentages of different batches recovered varied between 0·09 per cent. and 33·3 per cent.; the percentage of all releases recovered was 3·8 per cent. The times of recovery extended from one-eighth of a day when 8 were recaptured at 49·6 yards, to 21 days when one specimen was recaptured at 232 yards. The distances at which recaptures were made varied from 0 yards (at the point of release) where 57 were taken, to 475 yards where one specimen was taken; no marked mosquitoes were recovered beyond this distance though collecting was done up to 692 yards.

It is deduced from the figures presented that the ordinary range of flight activity of *Aëdes albopictus* is 200 yards or less and from the fluctuating numbers observed during the collecting that this mosquito travels in swarms, though more evidence is necessary regarding the latter point. It was noticed that this species flies near to the ground and the average rate of dispersal is calculated at about 15 yards per day. *H. S. Leeson.*

HATCHETT, S. P. **Winter Survival of *Aedes aegypti* (L.) in Houston, Tex.** *Pub. Health Rep.* Wash. 1946, Aug. 23, v. 61, No. 34, 1234–44, 2 figs. [11 refs.]

This investigation was made during the winter months November 1944 to April 1945. It was an unusually mild winter in Houston, Texas; the minimum temperature never fell below 30°F. and during March, and on eighteen other days, the maximum temperature reached 70°F.

About 10,000 eggs of *Aëdes aegypti* were under observation. Some were exposed for twenty-four hours to artificially cold conditions (26°F.) and then kept at room temperature. Half of them were kept continuously wet and half were dried for forty-eight hours before being immersed and exposed. No eggs hatched which were kept continuously wet, but 10 per cent. of those that had been dried did so. After forty-eight hours at 26°F. none hatched, but at 34°F. for twenty-four hours approximately half of the eggs hatched.

Other eggs were exposed to outdoor temperatures; some were immersed and some were kept dry throughout the winter, and others were alternately wetted and dried. On 3rd March all eggs were immersed and observed until 3rd April. Half of the eggs were in partially protected places and half in exposed situations. Among the eggs that had been continuously wet, 43·5 per cent. hatched; 21·4 per cent. hatched of those that had been continuously dry and 28·4 per cent. of those that were intermittently wetted. In general, those which were partially protected produced more larvae than those which were exposed.

The mean period of immersion before hatching was 32 days, but there was delayed hatching among eggs which had been immersed since early winter, whereas eggs which were immersed in February hatched more quickly. Among larvae which hatched out before 15th February, only 17 per cent. became adults but of 1,883 larvae closely observed throughout the winter 985 (52 per cent.) produced adults. Most of them took 2–3 weeks from the time of hatching to complete development and to emerge as adults but many died within 2 or 3 days. Most females which emerged after the middle of February lived long enough to mate, feed, and lay eggs.

Two susceptible stages were noticed; newly-hatched larvae and larvae about to pupate were more easily chilled than others. Another observation was that no individual lived that remained as a pupa for more than ten days.

From the point of view of control, the author points out that during mild winters special attention should be paid to the elimination of all small water receptacles as they may contain eggs of *Aëdes aegypti* which later may hatch out and produce adults. *H. S. Leeson.*

Agricultural Research Council. **Colonial Insecticide Research, Entebbe. Progress Report No. 1** [Symes, C. B., Entomologist-in-Charge]. 42 mimeographed pp., 2 maps (1 folding) & 3 plans. 1946. London: Inter-Departmental Insecticide Committees, Agricultural Research Council, 6A Dean's Yard.

Field and laboratory experiments have been commenced in Kenya, Uganda and on certain islands in Lake Victoria to determine the value of the insecticides DDT and gammexane for the control of the tsetse fly *Glossina palpalis*. This is a full report of work so far accomplished during 1945–46; as a result, several matters of practical importance are shown to need further elucidation. One of the chief problems is the loss of insecticide through absorption into the leaves of plants.

On one of the islands, a 5 per cent. solution of gammexane in equal parts of kerosene and cotton seed oil sprayed on vegetation at the rate of approximately 2·2 quarts per 1,000 square feet produced a reduction in the tsetse population of about 50 per cent. over some ten days; numbers then began to recover and about four weeks later had reached the pre-treatment figure.

A second spraying resulted in a reduction of the tsetse numbers by 80 per cent. for a week, but seven weeks later they were back again to 80 per cent. of the original figure.

On another island a trial was made with 5 per cent. DDT in equal parts of kerosene and cotton seed oil at the rate of 2 quarts per 1,000 square feet. An immediate reduction in the tsetse population of about 80 per cent. seemed apparent. This lasted for a week after when the numbers continued to increase, until by the sixth week they were back to the original figure.

On plants the leaves were still tacky after three weeks, non-hairy leaves showed little signs of burning, but the soft hairy-leafed plants had turned brown and died. Chemical determinations of deposits on these leaves indicated that there was appreciable loss of insecticides through absorption.

Laboratory tests of gammexane and DDT in kerosene, in kerosene and cotton seed oil and as dispersible powders showed that simple kerosene solutions burned the leaves and they dropped off. With kerosene-cotton seed oil solutions, plants were affected more or less seriously according to the type of leaf; tackiness lasted three weeks but absorption of the solution was considerable. The powders could still be seen after this time but they had little, if any, toxic effect on *G. palpalis*.

Comparison of the deposits of DDT on glass, wood, dried mud, grass and thatch showed that there was serious loss of insecticide on dried mud, thatch and probably on grass; the cotton seed oil tended to collect dust and debris, masking the insecticide. Dispersible powders gave good results on wood and on grassed mud but in 25 days had lost all toxicity to *G. palpalis*.

Field tests with DDT grenades were made by placing cages containing *G. palpalis*, ten to each cage, in various situations and allowing the smoke to pass over them. During the passing of the smoke, there was increased activity of the flies but the numbers dead after 24 hours were small. A second test with both gammexane and DDT grenades and with the cages placed 3 to 72 feet from the grenade and 18 inches to 2 feet above ground level knocked down all flies in 2 hours and in 24 hours they were all dead. Another test with the cages at intervals from the grenades of 4 to 60 yards and at 4 feet above ground level killed all flies in twelve hours, except a few in two cages nearest to the grenades; these were at 4 and 15 yards.

The results of these exploratory trials show that absorption of dispersible powders is not so great as that of solutions and emulsions; that deposits of insecticides on leaves vary with the leaf structure; that oil solutions applied to mud walls are wasteful; and that DDT and gammexane smoke kills tsetses if the smoke can be put where it is required.

The degree of solubility of gammexane and DDT in locally available solvents is given in a table. As soon as the supply of materials and equipment permits, further work is projected and will include investigation into the behaviour of these insecticides applied to the skin of cattle; the toxicity to calves; the effect on mosquitoes and on termites and an investigation into certain insect repellents. *H. S. Leeson.*

WOLFENBARGER, D. O. **Observations on the Airplane for Application of Sprays and Dusts.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 503–5.

"Swath width is seen as an important factor in the use of the airplane for spraying or dusting. More spray droplets and dust particles fell under the plane, and the droplet or particle numbers became less toward the margin of the swath covered. In comparing bottom and top slide surfaces the top surfaces received, on an average, over 90 per cent. of the spray droplets leaving very sparse coverings on the lower surfaces. Although aircraft have their place in distributing spray and dust materials, more research is necessary before definite conclusions may be drawn."

JACHOWSKI, L. A., Jr., & PIJOAN, M. **Two New Effective Insect Repellents, NMRI-201 and NMRI-448.** *Science*, 1946, Sept. 20, 266–9, 1 fig.

NMRI-201 consists of 70 per cent. 2-phenyl cyclohexanol and 30 per cent. beta-tetralol. As a repellent this mixture was more effective than either of the ingredients alone; other proportions were not so effective.

Tests were made in different parts of the U.S.A. and Central America against *Anopheles albimanus*, *Anopheles pseudopunctipennis*, *Aëdes taeniorhynchus*, *Aëdes aegypti*, and *Aëdes euplocamus*, using NMRI-201, 2-phenyl cyclohexanol,

dimethyl phthalate and citronella. NMRI-201 was effective for considerably longer periods than any of the other repellents not only against mosquitoes but also against mites and *Culicoides*.

Varying degrees of skin irritation were noted in 6 of the 59 subjects and though toxicity tests were generally favourable, continued administration to rabbits showed some toxicological manifestations due to beta-tetralol.

Other mixtures were then studied and eventually NMRI-448 was found to be even more effective than NMRI-201. This mixture consisted of 70 per cent. 2-phenyl cyclohexanol and 30 per cent. 2-cyclohexyl cyclohexanol. NMRI-448 has not been used by large numbers of people but so far no cases of skin irritation have been observed and toxicological tests, though as yet incomplete, indicate that NMRI-448 is likely to be acceptable for skin application.

H. S. Leeson.

Pijoan, M., Gerjovich, H. J., Hopwood, M. L., Jachowski, L. A. & Romine, J. T. **Studies on New Insect Repellents.** *U.S. Nav. Med. Bull.* 1946, Oct., v. 46, No. 10, 1506–22, 1 fig. [19 refs.]

This paper is concerned with the chemistry, methods of preparation and insect repellency of certain of the most effective compounds studied at the U.S. Naval Medical Research Institute. They are all hydrogenated naphthol derivatives and hydrogenated diphenyls and it is revealed that they are more effective than currently-used repellents and that mixing with 2-phenyl cyclohexanol results in a prolongation of their repellent activity. Toxicological tests are not yet complete. *Aëdes aegypti* was the test insect.

The repellents NMRI-201 and NMRI-448 were tested in the field also, in several parts of the United States and in Central America. The results of these tests are given in this paper and are the same as those already reported by Jachowski and Pijoan above. *H. S. Leeson.*

Bishopp, F. C. **The Insecticide Situation.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 449–59. [28 refs.]

Goodhue, L. D. **Aerosols and their Application.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 506–9. [15 refs.]

LABORATORY PROCEDURES.

Davies, G. E. & Fishburn, A. G. **The Testing of Drugs and Pharmaceutical Preparations for Sterility : a New Technique.** *Quart. J. Pharm. & Pharmacol.* 1946, July–Sept., v. 19, No. 3, 365–72, 2 figs.

The official sterility tests, *e.g.* those described in the British Pharmacopoeia, involve the addition of the sample of the material under test to broth ; and a drug is stated to pass the test if no growth of microorganisms is observable during an incubation period of five days. This procedure is unsatisfactory in many ways ; especially if the pharmaceutical preparation itself possesses bacteriostatic action, either this action will prevent growth of organisms which might still be viable in the body, or it will require high dilution, which will also dilute the hypothetical bacteria present. Accordingly a new technique is described in which the material to be tested is filtered through a sterile pad ; organisms present are thereby separated from the bulk of the pharmaceutical

preparation ; the pad is washed to remove the rest of the preparation, and the pad is then placed in a suitable culture medium to detect the presence of organisms. In more detail the procedure is as follows :—

(*a*) *Water-soluble drugs.*—Prepare a solution, if necessary, by dissolving the sample in sufficient sterile distilled water so as to give a concentration equivalent to that normally used for injection. Filter one-half of the solution through a sterile, plugged Seitz-filter fitted with a grade S.B. Sterimat (Ford's). The authors use a Sterimat 3 cm. in diameter so that the jar subsequently used for culture will not be too large. Wash the pad with 3×10 ml. amounts of sterile distilled water to remove the remaining portions of the drug. Then transfer the pad to a jar of aerobic broth. Repeat the process with the second half of the sample, this time transferring the pad to a jar of anaerobic broth. Incubate the jars at 37°C. for five days and examine daily for signs of growth.

(*b*) *Oils.*—Pour the sample into a sterile flask and add an equal volume of sterile light petroleum. Shake until homogeneous. Proceed as for water-soluble drugs, but use sterile light petroleum instead of water as the washing liquid.

The media recommended are :—

(1) For aerobic organisms :

Yeastrel	1
Peptone	1
Sodium chloride	0·5
Distilled water to	100

This is adjusted to *p*H 7·2 to counterbalance the slight influence of the pad.

(2) For anaerobic organisms :

Agar	0·15
Dextrose	1
Sodium thioglycollate	0·1
Methylene blue	0·002
" Aerobic " broth (as above) to	100

During incubation of the plugged jars the medium is covered with a layer of castor oil to prevent diffusion of oxygen, but this is unnecessary if screw-capped jars are used.

With certain bacteriostatic drugs of high potency the above number of washings may be insufficient and modifications may be needed. Thus, when a solution of penicillin containing 5,000 units/ml. was filtered and washed 6 times with 10 ml., the final fluid contained 2 units/ml. In this case, a penicillin-free filtrate was obtained by using 2×10 ml. washings with sterile water, followed by one 10 ml. washing with a sterile 2 per cent. solution of cysteine hydrochloride buffered to *p*H 7·6.

This new method is more sensitive than the official dilution one, and by its use bacteria were detected in ampoules (supplied as suitable for injection) of tryparsamide, thiopentone, and hexobarbitone soluble, but not in ampoules of mepacrine methane sulphonate or suramin. *F. Hawking.*

BRINDLE, H. & RIGBY, G. **The Preparation of Non-Pyrogenic Water and Infusion Fluids, using Activated Charcoal.** *Quart. J. Pharm. & Pharmacol.* 1946, July–Sept., v. 19, No. 3, 302–9.

Pyrogen is a thermostable product of the metabolism of certain strains of bacteria and is probably chemically related to their polysaccharide-bearing antigens. These antigenic products may develop in the distillate from ordinary water through the entrainment of bacteria, if it is allowed to stand unsterilized

for more than 24 hours. The distillate, too, when derived from a contaminated source may contain sufficient concentration of pyrogen to give a reaction even if it is sterilized immediately. A sharp rise in body temperature and a marked leucopenia constitute the pyrogenic reaction and the tests for pyrogen content are based upon these features. The minimum pyrogenic dose is defined as that dose per kgm. of body weight which causes a temperature response of 0·5 to 0·6°C. in rabbits. Removal of pyrogen is effected by shaking test water with 0·1 per cent. " Depyrogenising Charcoal " and a higher percentage than this would not be required for any contaminated water likely to be utilized in practice. The charcoal used for removal of pyrogen would also have an action by adsorption on active substances, such as glucose and sodium citrate, but the loss is slight. These drugs themselves, often used for injection, may be contaminating agents by containing pyrogen. Other methods tried out for " depyrogenising water ", such as chlorine, granular charcoal, autoclaving, and " filtration through a Doulton or ordinary Seitz asbestos bacteria proof pad " were unsuccessful. Storage for a period of six months of a sample of pyrogenic glucose resulted in freedom from active pyrogen. *W. F. Harvey.*

Turner, J. S., McLennan, E. I., Rogers, J. S. & Matthaei, E. **Tropic-Proofing of Optical Instruments by a Fungicide.** *Nature.* 1946, Oct. 5, 469–72, 3 figs.

In hot, moist climates, fungi are apt to grow over the lenses of optical instruments, deriving nutriment from particles of dust, luting wax or other material : eventually they may etch or stain the glass, with the result that ordinary cleaning is ineffective. The appearances produced are illustrated by photographs. During the recent campaign in New Guinea this became a serious problem, since binoculars, range-finders and cameras became unfit for use in large numbers within a few weeks, in store as well as in the field. A committee was established in Australia to investigate possible remedies. Many fungicides were tried and found useless, with the possible exception of thymol, but an apparently ideal one was found in sodium ethylmercurithiosalicylate. This suppressed the growth of all species of fungus concerned and, when incorporated in a concentration of 0·2 per cent. in a black lacquer used for coating the interior metal surfaces of optical instruments, was found to prevent fungal attack for months. How long its action persists has apparently not yet been determined. Experiments illustrative of its action are described. This substance also kills mites, although it does not repel them. Incorporated in a paint of the composition used, it does not corrode metals. [This paper is followed by two other notes on the same subject ; V. M. Trikojus dealing with the chemistry of this compound, and J. W. J. Fay, of the Ministry of Supply, commenting on the Australian findings somewhat guardedly. The aim in England has been to improve the sealing of instruments and to employ a desiccant, thus rendering the use of fungicide unnecessary.] *L. P. Garrod.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

Hinman, E. H. & Baez, M. M. **Opportunities for Training and Research in Tropical Medicine and Public Health in Mexico.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 529–37, 1 diagram.

Mexico is making great efforts to further the study and dispersion of knowledge of tropical disease and public health. Mexico lies between 15° and 32°

North latitude, but, owing to the mountains in its centre, the varieties of climate are great.

There is one Institute of Tropical Medicine, with 12 laboratories for research and a research hospital of 36 beds. It publishes its own review of work carried out there, the *Revista del Instituto de Salubridad y Enfermedades Tropicales*. Many of the researches being prosecuted are listed, including onchocerciasis, pinta, mycotic infections, typhus and infant diarrhoeas.

In 1942 a special hospital of 50 beds for the reception and study of onchocerciasis patients was opened at Huixtla, Chiapas, on the railway 48 kilometres from Tapachula. Since 1943 the Pan-American Sanitary Bureau has been cooperating in the onchocerca research. Opportunities for the study of pinta are great; it is estimated that there are some 300,000 cases in the country, and, owing to the disfigurement it produces, patients willingly and actively cooperate.

At Boca del Rio is a Health Centre and a Tropical Medicine Training Station which provides three types of service: First, a full-time Health Centre; second, a Field Research Station for the Tropical Institute mentioned above and third, a Field Training Station for those intending to engage in Tropical Medicine which takes doctors and those who have some knowledge of clinical tropical conditions and of laboratory work from Mexico, the United States and Latin America.

The Board of Health and Assistance also regulates study in nutrition, with a hospital of approximately 100 beds, apparently well-equipped and with laboratory facilities.

For more general health work there is a School of Hygiene (Escuela de Salubridad e Higiene) in Mexico City; this has been established since 1924, for the training of Medical Officers of Health, Nurses and Sanitary Inspectors. A new building was erected in 1939, with a large auditorium, three lecture rooms, five laboratories, a library, etc. The course for Public Health Officers extends over 40 weeks, in four equal periods, the last of which is devoted to field training, and special emphasis is placed on laboratory training in bacteriology, biochemistry and parasitology.

Health Centres are situated in various parts of the country, each having its staff of visiting nurses, out-patient dispensaries, dental service, etc. There are also several small basic training centres receiving three physicians, three nurses and six sanitation officers for a period of two months, and, if found satisfactory, they pass on for the fuller training course at the Mexico School of Hygiene. Mexico offers these facilities to students and research workers of countries other than her own. *H. Harold Scott.*

BOOK REVIEWS.

Russell, Paul F. [M.D., M.P.H., etc.], West, L. S. [Ph.D., etc.] & Manwell, Reginald D. [Sc.D., etc.]. **Practical Malariology. Prepared under the Auspices of the Division of Medical Sciences of the National Research Council.** Foreword by Raymond B. Fosdick. pp. xix + 684, 238 illustrations (8 in colour). 1946. Philadelphia & London: W. B. Saunders Company. [40s.]

This book opens with a foreword by Mr. Fosdick, the President of the Rockefeller Foundation, in which he writes, " We are living in the 20th Century and

we cannot retrace our steps back into the 19th. For better or for worse we find ourselves in an era in which our only hope of survival lies in collaboration across boundary lines." This need for collaboration, although it is not so stated, applies not only to nations but also to scientists, for malaria today has become a subject for intensive study by biologists as well as by doctors, nor can the work of chemists, physicists and engineers be neglected. It is appropriate therefore that this, the latest, and in the reviewer's opinion the best, book written on malaria should be the joint work of a doctor of medicine, a protozoologist and an entomologist. The aim of this trio is expressed in their preface in the following words, " The literature of malaria is vast and scattered. For some time there has been needed a book which would gather up the important features of malariology, integrating new developments with the old, and presenting a well-balanced account of this disease which, from the standpoint of prevalence, some authorities have called the most important in the world today."

That there is a real need for such a work can be proved by anyone who troubles to consult those books on malaria which have been published during the past 25 years. During this not inconsiderable, and certainly most productive, period of malaria history, a large number of books in many languages have been published on a variety of aspects of the disease, while several standard works on tropical medicine have appeared, and have contained good, but relatively incomplete, accounts of the malady and its vector. The only outstanding works, however, which have appeared during this period, which have concerned themselves solely with this subject, and which have considered it in all its important aspects, are limited in number, perhaps not more than half a dozen in all. The fact that these earlier volumes no longer fulfil their function, so that the modern worker on malariology must rely on the literature contained in periodicals, is rather a tribute to the progress of science, than any reflection on the ability of the authors. No doubt the same fate will eventually attend the volume at present being considered, but the reviewer predicts that it will reappear in more than one revised edition before it can no longer be re-patched and must become replaced by the work of a new generation. That what they have written is not to be considered as " the last word " is, of course, well known to Dr. Russell and his colleagues; indeed, one of the most stimulating features of their book is the attention paid to problems still awaiting solution.

The book is beautifully produced and magnificently illustrated ; over 200 of its 700 pages contain drawings, photographs or charts, while in the remaining space the authors have compressed their account of malaria, which deals with every aspect of the disease and the parasite, its vectors and its control. To fit so much information into so small a space will at once suggest over-crowding, over simplification, or else the omission of material vital to a proper understanding of the subject. To avoid these pitfalls must have proved a difficult task, which can only have been achieved by experienced workers determined to shift the scientific grain from the conjectural chaff. Truly, there are but few wasted words in this trenchant account, and it is possibly the authors' striving for verbal economy which has led them to omit a generally accepted " the " from many of their sentences ; thus on page 234 we read, " the tip of the point is bent downward slightly, usually by means of thumb-nail and the right side of thorax glued to the slanting surface." Such omissions are irritating to the average reader, particularly since the small space thus saved might have been less crudely gained by the avoidance of certain, admittedly rare, repetitions, such as the twice made explanation, in almost identical words, of " blue cloud " on page 44. But these trivial curtailments do little to mar a style that is always vigorous, clear cut and often vividly descriptive, as when the authors are writing of mosquito pupae, " A sudden shadow may send them tumbling to

the bottom ; " or even quietly humorous, as when criticizing the official mind, or describing the advantage of carrying a " net handle ". Nor does the economy of words result in the appearance of unsupported statements ; again and again the reader is struck with the authors' determination to see that each statement is substantiated by adequate references to its source. These references are tabulated at the end of each chapter, but there is no author's index and, since the total number of references exceeds 600, it is to be hoped that this omission will be rectified in later editions.

Amongst so much that is interesting and stimulating it is difficult to select examples, but the following are some typical points of interest taken from various sections. Writing of the malaria parasite, the authors state that there is some uncertainty whether it is within or on the surface of the host's cell, although the general opinion is that it is always intracellular. When describing the parasite, as seen in Giemsa-stained thick films, attention is drawn to the reddish halo or shadow which is sometimes seen surrounding the parasite. The authors consider that this may represent the remains of the reticulum of the host's cell, or of the Schüffner's dots, or both, and state that when seen, this appearance is diagnostic of *P. vivax*. [The reviewer also has noticed this characteristic, but found it equally common in *P. ovale* infections.]

The authors hold the commonly accepted view that in spite of all the experimental work which has been done on blood changes occurring in malaria, no diagnostic tests have yet been developed which equal in reliability the actual microscopic demonstration of parasites ; but they draw attention to the promising, but as yet unpublished, diagnostic tests based on recently devised techniques of complement fixation. In view of the attention recently paid to the value of sternal punctures in the diagnosis of malaria, it is interesting to read that " it is a consensus that they are not to be undertaken lightly by the inexperienced and that they are not useful in the diagnosis of malaria."

One of the most stimulating chapters in the book is that which deals with immunity, latency and relapse, but it does not lend itself to quotation *in extenso*, and it certainly cannot be further summarized. One paragraph, however, should be quoted, since it has a direct bearing on the author's views on prophylaxis and control. The paragraph in question reads as follows : " It appears to be true that early intensive treatment, begun as soon as parasites are found in a blood smear in a primary attack, will not permit a patient to develop much residual immunity if the treatment results in a radical cure. If he is completely cured he has lost nothing of practical importance, however, since any immunity he might otherwise have gained has little if any value in protecting against subsequent infection in nature. Even the partial immunity called tolerance is developed only by continuous attacks over a period of ten to fifteen years or more." That these remarks are intended to apply to the individual patient rather than to the community may be inferred from the following quotation made in a later chapter : " But with regard to the eradication of malaria in malarious communities by chemoprophylaxis it may be stated definitely and clearly that : (1) in spite of many attempts, this has never been accomplished ; (2) nothing in the record leads one to hope that this ever could be realized with drugs now available ; (3) except in times of an epidemic, the results achieved by mass therapy in malarious populations are usually not worth the effort or the cost ; (4) attempts at mass prophylaxis by drugs may do more harm than good by delaying more helpful antimosquito measures. Some observers believe that it may also interfere with a natural development of communal tolerance to the effects of malaria." When dealing with the life-cycle of the parasite in the mosquito, attention is drawn to the long incubation period of *P. malariae* in the mosquito, 4–5 weeks, required for the production of sporozoites, so that there is an excellent chance that the mosquito may not live long

enough to become infective, and it is suggested that if it were not for the extreme duration of quartan infection in man it is likely that this species of malaria might have become extinct long ago.

In the section on entomology, when writing of the migration of anophelines, attention is drawn to " the possibility that a species may adapt itself to a new climatic zone by utilization of a different altitude deserves investigation. This seems especially pertinent, since accidental transportation by man may now convey species over natural barriers which mosquitoes were formerly never able to cross." Later, the authors point out that since the methods of measuring the density and distribution of the vector have been so much improved, since the pioneer work of CHRISTOPHERS in 1911 and GILL in 1928, the subject of forecasting epidemics deserves further study. When discussing control measures it is interesting to find that the authors are in agreement with HACKETT's opinion that imperfect screening, no matter how bad, keeps out more anophelines than no screening at all, and that statements to the contrary are not supported by evidence.

Attention has already been drawn to frequent references in this book to problems still awaiting solution and a summary of the more important ones is presented in the preface in the following words: " Although the science of malariology is notably advanced, it is well to keep in mind certain lacunae which are still evident and which offer research problems of great interest. For example, we need to know much more concerning the biochemistry and physiology of the parasite, as well as about the hidden phases of its life-cycle. The perfecting of *in vitro* culture technic is urgently required. Our knowledge of malaria immunity is relatively scanty and not yet of much practical value. We are still ignorant of the nature of the tropisms which lead ovipositing anophelines to one type of water and not to another. Neither do we understand why man is attractive to some species and cattle to others. Our methods of measuring larval and adult densities, also of determining the degree of vector-contact with man, are crude. We have no completely prophylactic drug and we deal haltingly with therapeutic problems. Latency and relapses retain enigmatic characters. Prophylaxis has but recently progressed out of the blunderbuss stage."

The book ends with an appendix devoted to keys for the identification of adult and larval anophelines. Much of this work is taken from *Keys to the Anopheline Mosquitoes of the World*, with Dr. Russell as the senior author. This book has already been the subject of a review in this *Bulletin*, 1944, v. 41, 325.

The reviewer has little to offer in the way of criticism and only three suggestions, in addition to the few already made, for additional matter. It is rather surprising to find in a book so eminently practical no more than passing references to those artifacts and puzzles which are so often encountered by the novice in his search for the malaria parasite, and but little space would be taken by the introduction of an explanatory plate, similar to that illustrating the excellent description of artifacts given by KNOWLES and Senior WHITE in their " Malaria ". Those sections of the book dealing with field technique and malaria surveys are fine examples of well-balanced condensation, but more attention might be paid to the value of outdoor biting experiments when estimating malaria risk. An account of the concentration of the malaria parasite in the placenta is omitted and the effect of malaria on the pregnant female and on the child, before and after birth, somewhat neglected. These points might well be expanded in a later edition.

Dr. Russell and his colleagues may rest assured that wherever their travels may take them, they will find well-thumbed copies of their book, not so much

adorning shelves as lying on the work benches, of all those who are interested in the study of malaria. *R. M. Gordon.*

PAVLOVSKY, E. N. [Member of the Academy of Sciences and of the Academy of Medicine of U.S.S.R., Lieutenant-General of the Soviet Army Medical Service, Professor of General Biology and Parasitology in the Military Medical Academy, Laureate of Stalin's Premium, etc.] **Manual of Human Parasitology.** Vol. 1, 521 pp., 10 pls. & 375 text-figs. 5th Edition. 1946. Moscow-Leningrad. [Published by the Academy of Sciences of U.S.S.R.] [In Russian.] [44 Roubles.]

In 1924 the author published a short *Handbook of Human Parasitology*, which in its second edition (1934) appeared as a completely revised and amplified *Textbook of Human Parasitology* [this *Bulletin*, 1936, Vol. 33, 330]. According to the preface, the present edition, though ready for publication in 1940, was not issued until 1946. However, in the intervening six years—*during the war*—there appeared two abridged versions of this book. To preserve chronological continuity, the present edition is referred to as the fifth, but the 1940 text has remained unchanged.

The present edition of Pavlovsky's *Manual of Human Parasitology*, while covering the same ground as the second edition, has expanded considerably and is now brought out in two volumes, of which this is the first one.

This volume is devoted to the protozoa and helminths. In the introductory section a detailed account is given of the general conceptions of parasitology, with special emphasis on its ecological aspects and host-parasite relationships. The special sections deal with all the more important parasites of man. A description is given of their morphology, life-history and effect upon the host. In the case of malaria parasites and helminths, standardized methods of prophylactic and therapeutic treatment are also adduced. This text-book is primarily adapted to the needs of Soviet Public Health and of the Red Army. As the only comprehensive treatise on medical parasitology in the Russian language, written by its foremost exponent in U.S.S.R., it will doubtless enjoy the same high reputation as its predecessor. The book is illustrated by numerous text-figures and coloured plates but, unfortunately, some of the latter have suffered in reproduction. The bibliography contains references to Russian works exclusively. The alphabetical indices are on a lavish scale, comprising Russian and Latin names of animals, authors' names, subject index, geographical and ethnographical index, and an index of Latin terms. *C. A. Hoare.*

WAR OFFICE. **Manual of Chemistry for Dispensers.** W.O. Code No. 1612. 206 pp., numerous figs. 1931 (Reprinted 1946). London : H.M. Stationery Office. [3*s.* 6*d.*]

This manual should prove of value to those charged with giving instruction in elementary chemistry and physics to medical and other students in the training schools of tropical dependencies.

Explanations are given clearly, experimental examples of natural phenomena are easy to follow and illustrations are simple and understandable. Nevertheless, the manual includes " such general practical knowledge of elementary chemistry and physics as will enable a student dispenser to understand the main principles of pharmacy and of the first-aid treatment of poisons."

H. J. O'D. Burke-Gaffney.

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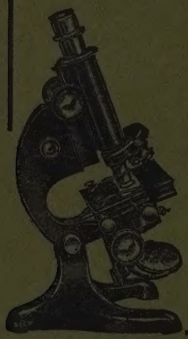

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